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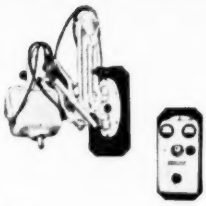

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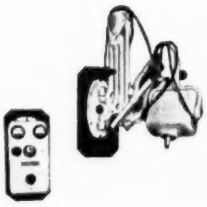

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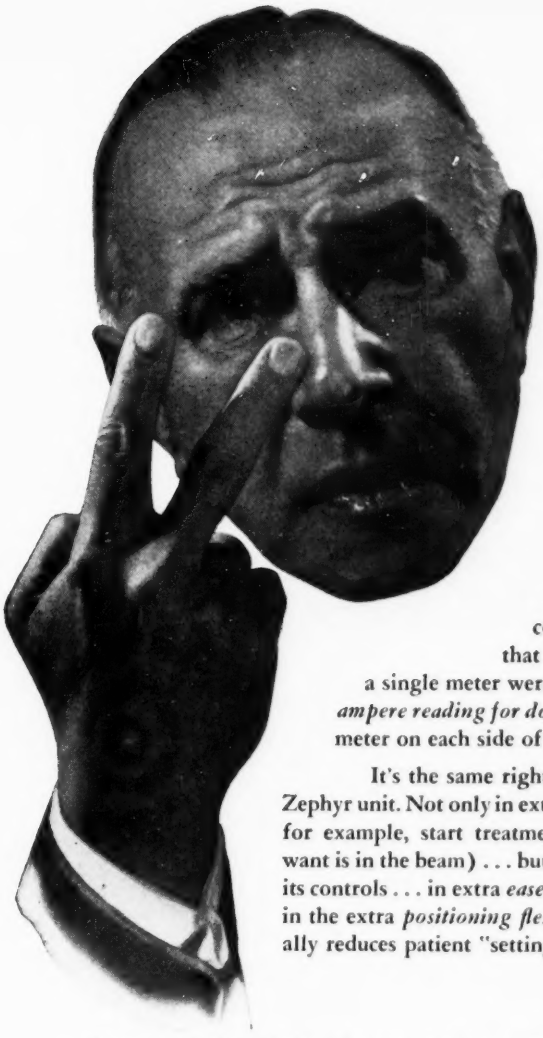

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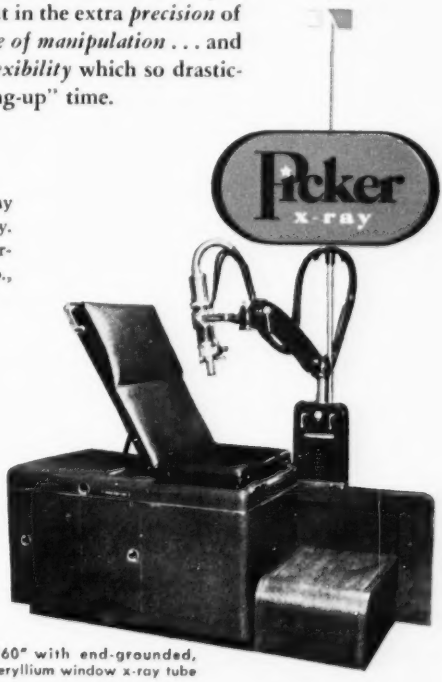

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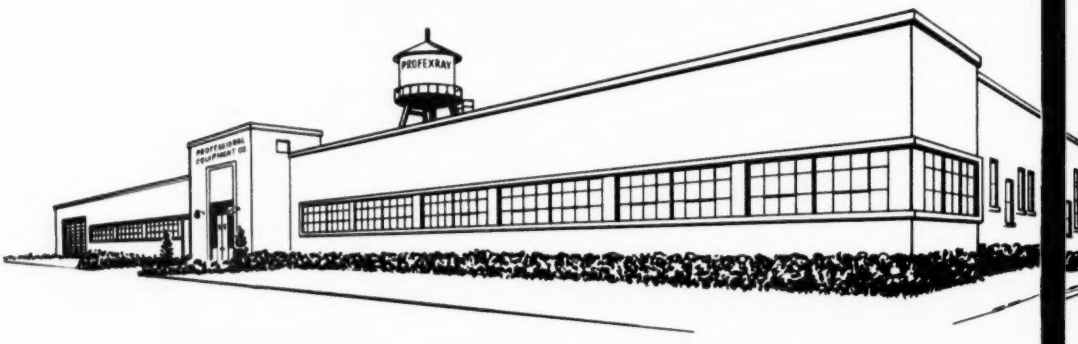

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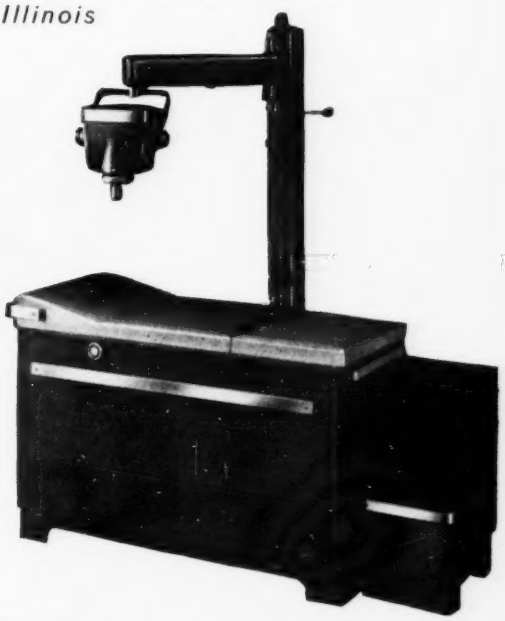

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1. Rhoads, P.S., *GP* 5:67, February 1952.

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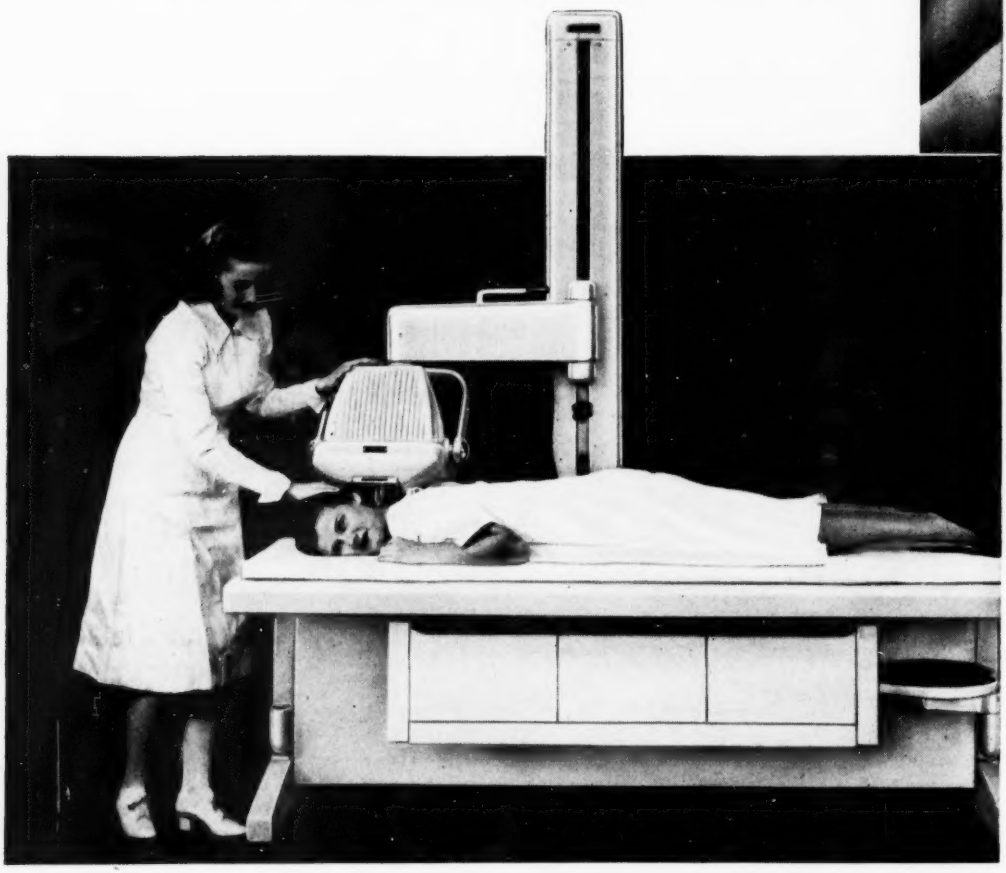

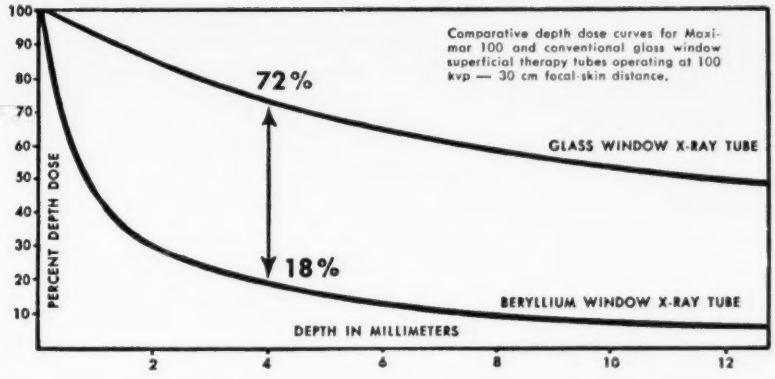

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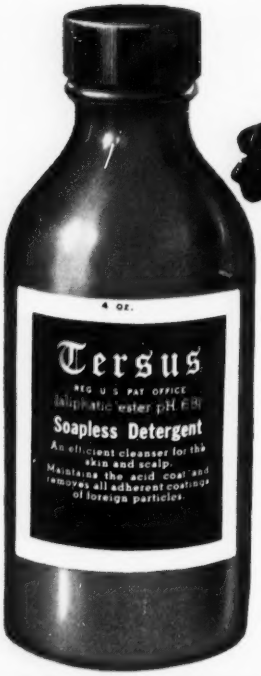
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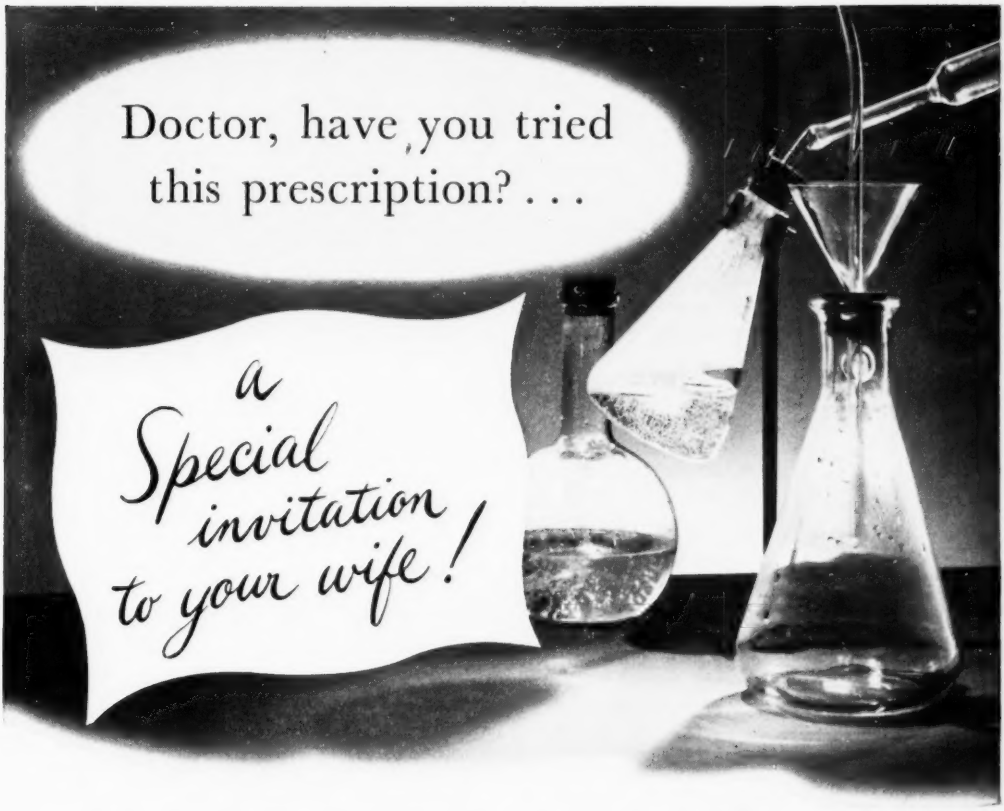

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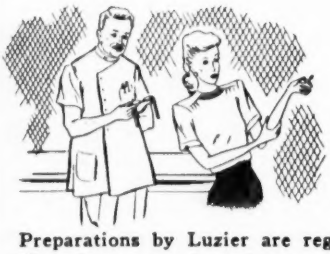

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BENIGN INOCULATION LYMPHORETICULOSIS (CAT-SCRATCH DISEASE)

Report of Two Cases with Positive Skin Tests

JAMES JAMBOR, M.D.
AND
EDWARD EMURA, M.D.
CINCINNATI

SINCE the first published report of this disease under the name *maladie des griffes de chat* by Debré,[1] reports of this disease in widely separated areas of the world indicate its widespread distribution and not infrequent occurrence. Because of the clinical manifestations, benign inoculation lymphoreticulosis may mimic other disease processes within the province of the dermatologist [2] and must enter into several differential diagnoses, as is illustrated by the two cases here reported.

As described in previous reports, benign inoculation lymphoreticulosis is a self-limited disease involving a group of regional lymph nodes depending upon the site of inoculation.[3] After some minor trauma to the skin, frequently but not necessarily the scratch of a cat,[3] at the inoculation site a small ulcer may develop within two to four days; it may become manifest only at the time of the development of the lymphadenopathy, or it may remain latent during the course of the infection. Within two to four weeks after the inoculation, regional lymphadenopathy occurs. This may be marked and may be associated with moderate fever and malaise,[4] as is noted in our patients. The nodes may persist without suppuration for months, gradually regressing in size, or they may suppurate and discharge the necrotic material through the skin. Depending upon location, the process may mimic tuberculous adenitis with scrofuloderma as in Case 1, or lymphogranuloma venereum as in Case 2.

Although culture has not been successfully carried out,[5] and though there is not a frequent cross immunity to other members of the psittacosis-lymphogranuloma

From the Department of Dermatology and Syphilology of the College of Medicine of the University of Cincinnati.

1. Debré, R.; Lamy, M.; Jammet, M. L.; Costil, L., and Mozziconacci, P.: La maladie des griffes de chat, Bull. et mém. Soc. méd. hôp. Paris **66**:76-79, 1950.

2. Epstein, E.: Cat-Scratch Fever, A. M. A. Arch. Dermat. & Syph. **66**:240-243, 1952.

3. Mollaret, P.; Reilly, J.; Bastin, R., and Tournier, P.: Documentation nouvelle sur l'adénopathie régionale subaiguë et spontanément curable décrite en 1950: La lymphoréticulose bénigne d'inoculation, Presse méd. **58**:1353-1355, 1950.

4. Daniels, W. B., and MacMurray, F. G.: Cat-Scratch Disease: Nonbacterial Regional Lymphadenitis, A. M. A. Arch. Int. Med. **88**:736-751, 1951.

5. Foshay, L.: Personal communication to the authors.

venereum group of viruses, the relationship is supported by present evidence. The pathology is strikingly similar to that of lymph nodes from a case of Nicholas-Favre disease.[6] There is an early lymphocytotic infiltrate in and around the capsule of the node associated with reticuloendothelial hyperplasia, followed by necrosis and stellate microabscess formation, leading in some cases to massive necrosis and destruction of the normal architecture of the node.

Sections of the nodes and the primary lesions from both man and the Cercopithecus ethops sabaeus monkey infected by material from the node of a human patient, when prepared with Mann's stain, reveal oxyphilic intranuclear and intracytoplasmic inclusion bodies. Giemsa's stain reveals basophilic bodies in the cytoplasm of lymphocytes, plasma cells, and reticulocytes. These bodies are especially numerous in early lymph node lesions and are considered to represent the virus.[7] Although the disease is believed to be self-limited and benign, the rapid involution of the lesions in one patient treated with chloramphenicol and the failure of five patients to respond to penicillin suggest further the relationship between this disease and the lymphogranuloma venereum group of viruses.[4]

The diagnosis is made by a skin test which is apparently specific for this disease and negative in controls. The antigen was originally prepared as Frei prepared his antigen, by diluting pus from a bubo with isotonic saline solution 1:5 and tyndallizing it on two successive days. However, macerated necrotic tissue from a lymph node similarly handled gives a good antigen.[4] Antigen from a patient with known benign inoculation lymphoreticulosis inoculated intradermally into the suspected patient should give a reaction of a papule 5 mm. in diameter after 48 hours, to be read as positive. Or an antigen may be prepared from the patient's own material and injected into a previous patient, a procedure similar to the reverse Frei test.

REPORT OF CASES

CASE 1 (Fig.).—A 12-year-old white girl had been scratched on the right side of the neck by a cat on Oct. 1, 1950. This was an insignificant trauma, and the lesions healed readily. On Oct. 11, three small (3 mm. in diameter) papules appeared at the site of the scratches. These formed a crust and were so trivial that the patient thought them to be insect bites and treated them with a proprietary antiseptic. The lesions seemed to be regressing, when 20 days after the cat scratch small tender lymph nodes became manifest on the right side of the neck beneath the points of inoculation. These nodes gradually enlarged. The child was admitted to the Children's Hospital. Twenty-seven days after the inoculation, the patient was given a dose of 300,000 units of procaine penicillin daily. There were no symptoms of malaise, although she had a fever which reached 102 F. on the 32d day and which gradually fell to the normal temperature by the 35th day. At this time, the nodes in her neck formed two masses which measured 4 by 6 cm. and 3 by 4 cm. and were warm and tender. The patient was seen in consultation by Dr. Lee Foshay, who concurred in the impression of cat-scratch disease and furnished antigen for skin testing. The result of the skin test with cat-scratch antigen at this time was positive, producing a 6-mm. papule at the end of 72 hours. On the 42d day of the

6. Daniels, and MacMurray.[4] Mollaret, P.; Reilly, J.; Bastin, R., and Tournier, P.: Sur une adénopathie régionale subaiguë et spontanément curable, avec intradermo-réaction et lésions ganglionnaires particulières, Bull. et mém. Soc. méd. hôp. Paris **66**:424-449, 1950.

7. Mollaret, P.; Reilly, J.; Bastin, R., and Tournier, P.: La découverte du virus de la lymphoréticulose bénigne d'inoculation: Caractérization sérologique et immunologique, Presse méd. **59**:681; Inoculation expérimentale au singe et colorations, ibid. **59**:701, 1951.

disease, suppuration occurred, and 5 cc. of thick sanguineopurulent material was obtained by aspiration. This material was sterile as determined by cultures for bacteria and fungi. A smear of this material stained with Machiavello's stain revealed many polymorphonuclear leucocytes with small red round and elongated bodies about the size of elementary bodies seen in psittacosis. Hematologic and other laboratory findings were normal. After the aspiration of pus from the suppurating nodes, the nodes gradually decreased in size but were still palpably enlarged four months after aspiration.

CASE 2.—A 14-year-old Negro girl, admitted to the service of dermatology and syphilology of the Cincinnati General Hospital, noticed a lump in the right inguinal fold in early August, 1951. This remained asymptomatic until two weeks later, when it became tender. At the same time she began experiencing headache, chilliness, fever, malaise, and anorexia. These symptoms gradually became worse until she came to the hospital. At the time of admission there was a

Left, profile view showing the scrofula-like swelling of the right cervical lymph nodes; right, small crusted papules resembling the puckered sinuses of scrofuloderma. Discoloration due to local antiseptic.

tender mass of femoral lymph nodes on the right, measuring 8 by 6 cm., and a small red crusted papule on her right crus which she had thought was an insect bite. Further questioning elicited the fact that there were several cats in her home, and that she was frequently scratched on her legs, and that this might represent a scratch. On Sept. 6, the date of admission to the hospital, the temperature was 103.4 F., the pulse rate was 120 per minute, and the patient appeared acutely ill. She was extremely lethargic and somnolent and gave equivocal signs of meningeal irritation. Lumbar tap was performed, yielding a completely normal spinal fluid under normal pressure. On admission her leucocyte count was 18,350 cells per cubic millimeter, falling to 8,900 the next day. Because of a gonorrheal cervicitis, she was given 2,400,000 units of penicillin the day of admission. The temperature fell to normal gradually over a period of 10 days, with simultaneous diminution of lethargy.

During her hospital stay of one month repeated Frei tests, serologic tests for syphilis, tularemia agglutinations, blood cultures, cultures of serum aspirated from the femoral nodes for

both acid-fast and non-acid-fast bacteria gave negative results. The patient was seen in consultation by Dr. Lee Foshay, who concurred in the impression of cat-scratch disease. On Sept. 15 and on Oct. 15, skin tests with cat-scratch antigen showed a positive reaction. During her month of hospitalization the nodes failed to suppurate but slowly decreased in size. On Oct. 15, the mass measured 3 by 3 cm. and was nontender and firm. Six months after her discharge the size of the nodes had not changed.

SUMMARY

Two cases of benign inoculation lymphoreticulosis (cat-scratch disease) as proved by positive skin-test reactions are presented, illustrating the protean manifestations of the disease and the necessity of differentiating it from tuberculous cervical lymphadenitis, tularemia, and especially from lymphogranuloma venereum, which it mimics both clinically and pathologically.

Dr. Worth B. Daniels, Dr. Vinton Sneeden, and Dr. Lee Foshay furnished the antigen which enabled us to perform the intradermal tests.

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WILBERT SACHS, M.D.
NEW YORK

OPINIONS differ as to the nosology of the bullous type of congenital ichthyosiform erythroderma. The pertinent questions that arise regarding this disease are the following: Is it a variant of the nonbullous type? Are the bullae due to a superimposed infection? How is it clinically and histologically related to other dermatoses of the ichthyosis group? Or, finally, is the infection a combination of ichthyosis and epidermolysis bullosa?

In an endeavor to answer these questions we have searched the literature on congenital ichthyosiform erythroderma for examples of the bullous form and have found only 19 such cases reported. Presented here is a history of a typical bullous case which has been under our observation for the past 18 months. A synopsis of the clinical and pathological findings in the 19 cases previously reported is also given.

CASES IN THE LITERATURE

As first described by Brocq,[1] in 1902, congenital ichthyosiform erythroderma occurred with or without bullae. In the extensive review of the literature contributed by MacKee and Rosen,[2] in 1917, 12 of the 45 cases recorded therein are of the bullous type. Of the 16 cases reviewed by Weiss and Tobias,[3] in 1925, the description of only 1 included bullae—attributed to a secondary infection. The 1926 Goeckerman [4] report added two cases of the bullous variety.

Since this last study, only four complete reports of congenital ichthyosiform erythroderma have appeared in the English literature,[5] although other cases have been recorded in the transactions of the various American dermatological societies. Of these, bullae were present in only two.[6]

Read at the Seventy-Second Annual Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo., April 23, 1952.

1. Brocq, L.: Erythrodermie congénitale ichthyosiforme avec hyperépidermotrophie, Ann. dermat. et syph. **3**:1-31, 1902.

2. MacKee, G. M., and Rosen, I.: Erythrodermie congénitale ichthyosiforme, J. Cutan. Dis **35**:235-251, 343-361, and 511-540, 1917.

3. Weiss, R. S., and Tobias, N.: Congenital Ichthyosiform Erythroderma, Arch. Dermat. & Syph. **12**:182-194, 1925.

4. Goeckerman, W. H.: Bullous Ichthyosiform Erythroderma, Arch. Dermat. & Syph. **14**:158-172, 1926.

5. Lawless, T. K.: Congenital Ichthyosiform Erythroderma, Arch. Dermat. & Syph. **44**: 30-36, 1941. Laymon, C. W., and Murphy, R.: Congenital Ichthyosiform Erythroderma, ibid. **57**:615-624, 1948. Vukas, A.: Erythroderma Ichthyosiforme Congenitum: Epidermotectoscopical Description of Case, ibid. **64**:36-40, 1951. Fitzgerald, W. C., and Booker, A. P.: Congenital Ichthyosiform Erythroderma: Report of Two Cases in Siblings, One Complicated by Kaposi's Varicelliform Eruption, ibid. **64**:611-619, 1951.

6. Asel, N.; Chivington, P., and Spiller, W.: Congenital Ichthyosiform Erythroderma, A. M. A. Arch. Dermat. & Syph. **64**:79-80, 1951. Curtis, G. H.: Bullous Congenital Ichthyosiform Erythroderma in a Girl Aged 17 Years, A. M. A. Arch. Dermat. & Syph. **64**:80-81, 1951.

Under different cognomens four additional descriptions have been published, which we believe would be better named bullous congenital ichthyosiform erythroderma. Goldsmith,[7] in 1928, reported a case as "Congenital Keratoses with Bullae," which he cited as a "good example of the hystrix variety of congenital ichthyosiform erythroderma." Also in 1928, Macleod[8] recorded two cases as "Ichthyosis Bullosa." Reyes,[9] in 1945, described a case under the title, "Epidermodysplasia Hystricoidis Bullosa."

REPORT OF A CASE

History.—A 7-year-old white girl was born six weeks prematurely in the United States of Irish parents, who are not blood relatives. The father, aged 46, has had congenital ichthyosis hystrix of the linear type on the entire trunk and extremities, including the hands, feet, and shaft of the penis. (The mother and the two other children, aged 9 years and 1 year, have normal skins.)

At birth bullae were present on the patient's skin, and during her first year the entire cutaneous surface became erythematous and scaly. Through the ensuing years she has never been free of bullae, which are more numerous in winter. Her ichthyosis has increased, but the erythroderma has remained unchanged. No abnormal growth of hair or nails has been noticed. The child has not perspired in the winter except on the palms, soles, and sides of the nose. For several months prior to our examination she received vitamin A orally, with no resultant improvement.

Physical Examination.—Physical examination showed the child to be underweight but normal, except for the generalized scaly, erythematous, and bullous eruption. Scaliness varied from scanty patches on the face to thickened coarse ichthyotic areas on the abdomen, elbows, knees, and the dorsa of the hands. In the axillae, around the neck, in the groin, and in the popliteal and antecubital spaces, the skin was dark brown and verrucous, forming elevated cornified ridges. There were several unruptured and many ruptured bullae on the trunk and extremities (not limited to the pressure areas). None were present on the face, palms, or soles, which were red and moderately hyperkeratotic. The scalp was covered with thick greasy scales. Hair, nails, eyes, teeth, and mucous membranes appeared normal. The Nikolsky sign could not be produced.

Course.—During our 18 month observation of the patient, she was hospitalized for two explosive outbreaks of bullae, which were accompanied by moderate elevations of temperature. Complete laboratory studies were made and various treatments tried.

In the first hospitalization, September, 1951, her temperature ranged between 100 and 102 F. Numerous flaccid bullae developed and ruptured early. Cultures for bacteria from unruptured bullae yielded no pathogens, but Staphylococci were recovered from ruptured lesions. Penicillin and aureomycin were administered for four days, after which penicillin and chloramphenicol were given for two days. Neither of the treatments influenced the temperature or the eruption of new bullae. The patient was sponged with potassium permanganate solution, and bacitracin ointment was applied to the eroded areas.

On the seventh day corticotropin was given, 15 mg. every six hours for eight days (total dose 450 mg.), and penicillin was continued. On the fourth day after corticotropin administration the temperature dropped to normal, but under corticotropin therapy the bullae multiplied, leaving large denuded patches, especially over pressure areas. These erosions showed little tendency to heal until corticotropin was discontinued. The Nikolsky sign, definitely negative before corticotropin was given, was now easily elicited with the slightest trauma. When the patient was discharged on the 23d hospital day, a few bullae were still forming. The Nikolsky sign was more difficult to produce and was absent when she was again hospitalized two months later.

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7. Goldsmith, W. N.: Congenital Keratoses with Bullae, Brit. J. Dermat. **40**:59-77, 1928.

8. Macleod, J. M. H.: Note on 2 Cases of Ichthyosis Bullosa, Brit. J. Dermat. **40**:51-58, 1928.

9. Reyes, J. G.: Epidermodysplasia Hystricoidis Bullosa: Report of Case with Histopathologic Study, Arch. Dermat. & Syph. **52**:328-334, 1945.

Fig. 1.—Patient with generalized dryness of skin and with verrucous thickening in antecubital space, groin, and neck. Note also ruptured bullae on right arm, right side of trunk, and inner aspect of thighs.

The clinical course during the second hospitalization was similar to the first, except for considerable secondary cutaneous infection, which was probably due to hygienic neglect. The temperature returned to normal after three days of penicillin therapy, and the secondary infection cleared promptly.

Laboratory Study.—Blood tests for sugar, potassium, sodium, urea nitrogen, creatine, cholesterol, and serum proteins showed nothing abnormal throughout the two attacks. The leucocyte count was elevated to 11,000 (normal differential count) only during the febrile stages. There was a moderate secondary anemia. Urinalysis revealed no abnormalities. The 17-ketosteroid test, performed in the second hospital period, also showed normal findings.

Fig. 2.—Linear type of ichthyosis hystrix on legs of patient's father.

Neuropsychiatric study failed to demonstrate any disturbance, and the child was reported to be above average intelligence.

Since the second discharge, the patient has received biotin injections, 5 mg. three times a week for eight weeks. She feels better, and now has bullous-free periods. There is no change in the redness and dryness of the skin. The patient remains under observation.

HISTOLOGIC STUDY

Specimen from Thickened Skin of Antecubital Space.— Figure 3 shows that the epidermis is thickened and the surface verrucous and covered with an increased loosely laminated horny layer. Beneath this is a definite stratum lucidum. The underlying granular layer is accentuated; the cells are ballooned; the nuclei well

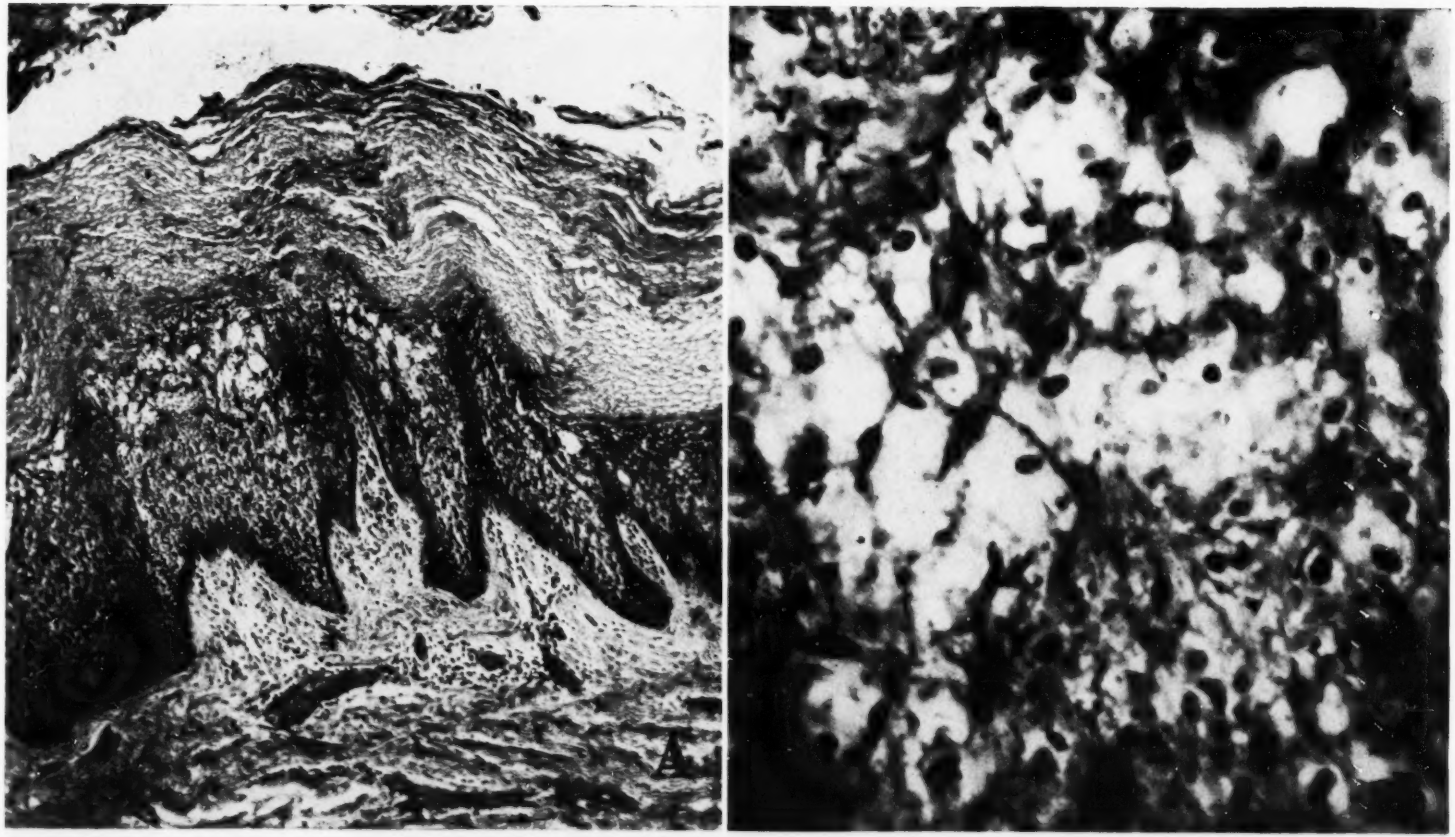

Fig. 3.—*A*, low power photomicrograph (patient) showing ballooning of granular layer and tremendous lossely laminated horny layer; also slight superficial inflammatory reaction. *B*, high power photomicrograph (patient) showing balloo ning of granular layer and silght amount of granules in the cells.

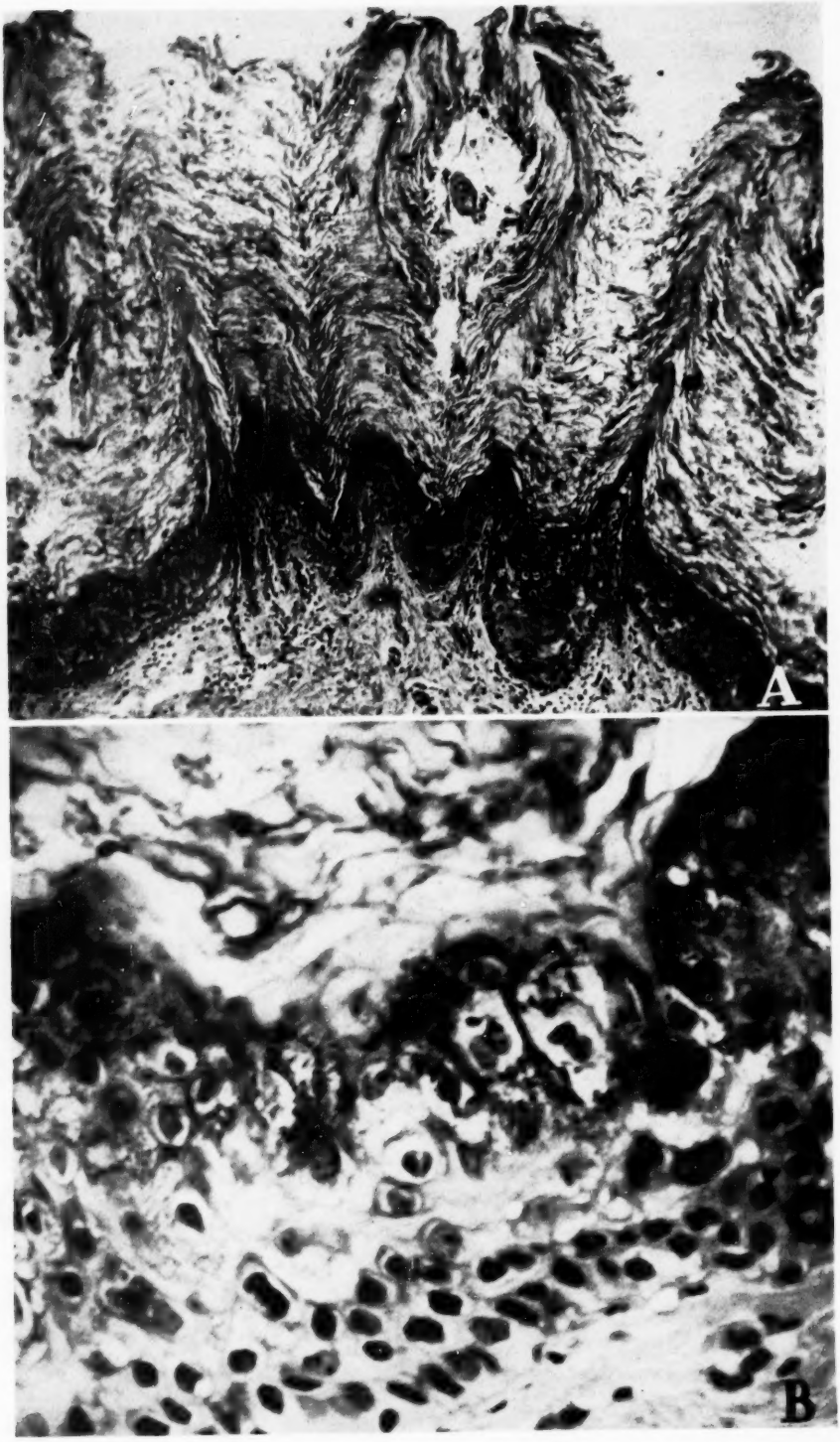

Fig. 4.—*A*, low power photomicrograph (patient's father) showing changes in granular and horny layers (ichthyosis hystrix). *B*, high power photomicrograph (patient's father) showing ballooning of cells of granular layer and large size of granules.

formed and stained, and the cytoplasm represented by clear spaces in which there are granules. These granules are not particularly numerous nor especially distinct. Where present, they are usually much larger than normal. The entire granular layer gives the general appearance of a peculiar retiform pattern similar to that seen in epidermodysplasia verruciformis. The basal and prickle cell layers show no abnormality.

In the subepidermic region is a mild inflammatory reaction; the vessels are slightly dilated and a sparse small, round, and wandering connective-tissue cellular infiltration is noted. A mild interstitial edema can be seen throughout the cutis. The adnexal tissue is present; there is no apparent diminution in number or size of the sweat apparatus or follicles.

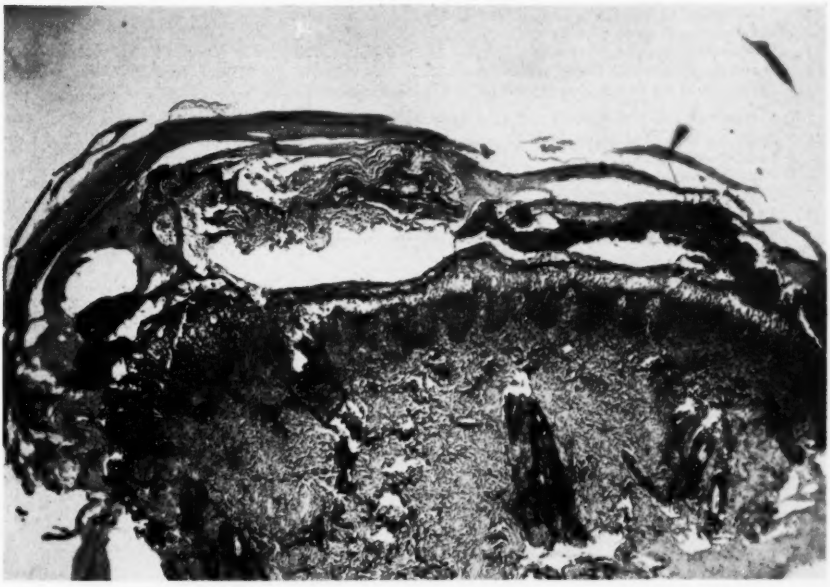

Fig. 5.—Section through an unruptured bulla showing bullous formation in and above the granular layer.

Specimen from an Unruptured Bulla.—The cells comprising the granular layer are enormously ballooned, and a bulla is forming in and extending above the granular layer. The surface shows some crusting, and some polymorphonuclear leucocytes are present. Since clinically this lesion was an unruptured bulla and microscopically the bulla developed in the granular layer, we must assume that the bullae in this disease are intraepidermic.

Specimen from Ichthyosis Hystrix of Father.—This specimen shows features similar to those seen in Figure 3, except that the granular layer, while of a definitely retiform pattern in places, is not as pronounced. This slide shows the characteristics of ichthyosis with some of the changes designated as epidermodysplasia.

A synopsis of the clinical findings in 19 cases reported with bullae is as follows:

	Cases
Sex prevalence	
Males	10
Females	9
Family histories	
Syphilitic mother	1
Syphilitic father and mother with psoriasis	1
Related parents, first cousins	1
Similarly afflicted siblings	3
Similarly afflicted siblings who died in infancy	2
Age of onset	
At birth	10
Onset during early childhood (13 mo., 2, 5, 6, 7 yr., respectively)	5
Not reported (Precedence of symptoms, no consistency)	4
Ichthyosis	
Xerosis and scaliness of varying degrees	All cases
Involvement of trunk and extremities	19
Greatest involvement of flexors	7
Greatest involvement of extensors	4
Equal involvement of flexors and extensors	3
No report of amount of involvement of flexors and extensors	5
Erythroderma (the most variable and least described symptom)	
Slight or only after exfoliation	3
Generalized	3
Limited areas, i. e., extremities, neck, abdomen, thorax	5
Distribution not mentioned	7
Seasonal variation, worse in winter	2
Improvement with age	7
Bullous manifestations	
In crops, with fever from a few hours to 10 days	7
Accompanied by abscess formation producing denuded areas	2
Present at most times	2
Worse in winter	2
Only in summer, believed due to sweating	1
No mention	8
Limited to pressure areas	5
Improvement with age	4
Nikolsky sign reported (1 positive, 1 not present)	2
Hidrosis	
Diminished (one perspired normally in summer)	7
Excessive where hyperkeratosis was worst	1
Excessive on palms and soles	2
Excessive on face	1
Involvement of specific areas	
Palms and soles	
Redness with scaling to thickened hyperkeratosis	9
Normal	3
Not reported	7
Face	
Slight to moderate redness	16
Normal	1
Not reported	2
(Bullae appeared on face in some instances, but not consistently)	
Scalp	
Slight scaling to thick crusting or seborrhea	10
Normal	5
Not reported	4
Hair	
Rapid growth	3
Normal	3
Not reported	10
Scanty growth	2
Absence of body hair, normal scalp	1
Excessive hair on body (buttocks, thighs, and neck)	1

Nails	
Abnormal growth	6
Normal	2
Bulbous	1
Not reported	10
Teeth	
Caries	1
Irregular	1
Normal	1
Not reported	16
Eyes	
Ectropion	3
Redness	1
Not reported	15
Mucous membranes	
Dryness of mucosa of mouth	2
Mental and physical development	
Below par mentally and physically	2
Below par mentally, normal physically	2
Recorded treatment	
Results of roentgen therapy (3 cases)	
Improvement of redness and thickening of palms	2
Disappearance of bullae on dorsa of hands and feet for four years and improvement after recurrence	1
Results of internal medication	
No influence on disease of arsenic, vitamin D with calcium, undecylenic acid, iron, and sulfapyridine	1

SYNOPSIS OF HISTOLOGIC FINDINGS

The following summary from MacKee and Rosen appears to represent the consensus of the above findings. In the description of the pathology in their large series of cases, they found no microscopic differences between the bullous and the nonbullous forms. Their histologic studies stress (1) the increase in the horny layer, at times extending into the hair follicles; (2) an occasional mild acanthosis; (3) a slight to moderate inflammatory process, and (4) an inconstantly reduced or fragmented elastic tissue.

While the above pathological features are emphasized, MacKee and Rosen state, however, that "occasionally a peculiar type of edema or dyskeratosis is encountered."

Clinical Comparison of Nonbullous and Bullous Congenital Ichthyosiform Erythroderma.—The history in the case presented and the synopsis of previous cases illustrate that the over-all clinical picture of the bullous form of congenital ichthyosiform erythroderma is similar if not identical to the nonbullous, the only variation being the presence of bullous lesions. Both forms appear either at birth or during early childhood, prevail equally in both sexes, seem to be familial but not hereditary, and are characterized by erythroderma and generalized (occasionally patchy in nonbullous only) hyperkeratosis of the skin. These characteristic symptoms vary in extent and severity, the hyperkeratosis having a tendency to progress and the erythroderma to regress. The ichthyotic changes range from slight xerosis to excessively coarse, dry, and verrucous thickening suggestive of the porcupine skin seen in ichthyosis hystrix. This thickening is most likely to occur in the axillae, in the groin, around the neck, and in the antecubital and popliteal spaces.

Hidrosis, usually diminished on the body, may be increased on the palms, soles, face, and thickened areas.

Palms and soles, when affected, show hyperkeratosis and erythema. The face, always least involved, may be red, shiny, drawn, and scaly. Ectropion has been reported. Scalps may be normal or have dry or greasy scales. Hair and nails may grow naturally, rapidly, or slowly.

Erythroderma may appear over the entire body, although it is commonly most obvious on the face, neck, and body folds. In some instances it is noticeable only in limited areas or after exfoliation.

In a few cases of congenital ichthyosiform erythroderma, bullous or nonbullous, there are associated minor congenital anomalies of teeth and ears. Also, cutaneous horns, nevi, and a bald patch on the scalp have been recorded. Mental and physical deficiencies are rarely encountered.

When the disease is bullous, the lesions appear in crops, with or without fever, or a few at a time, with rare bullous-free periods. Bullae may be present on any part of the body except the palms, soles, and mucous surfaces. In some instances they develop only over pressure areas. There is no consistent seasonal influence.

No therapy (with the exception of favorable results from roentgen therapy reported in two cases) has been efficacious in either bullous or nonbullous congenital ichthyosiform erythroderma.

COMMENT

On the basis of our study we shall attempt to clarify the essential differences of opinion in regard to the classification of bullous congenital ichthyosiform erythroderma as cited in the introduction.

Is the Disease a Variant of the Nonbullous Form?—The clinical and microscopic findings, according to the literature, are the same in both bullous and nonbullous forms. We agree with this concept. The presence of bullae does not change the character of the disease any more than the bullae in lichen planus or lupus erythematosus alter the diagnosis of these dermatoses.

Are the Bullae Due to Superimposed Infections?—Secondary infection does not explain the formation of bullae. They are often present without fever. The lesions are bullous rather than pustular and may become less numerous or cease to develop with age. Antibiotics and sulfonamides thus far have not influenced their course, nor before the days of the antibiotics were any patients reported to have succumbed to such an extensive infection.

The microscopic picture is not that of a pustule or an impetiginous lesion.

How Is It Clinically and Histologically Related to Other Dermatoses of the Ichthyosis Group?—Certain clinical features of ichthyosis are present, and in some instances the spinous excrescences resembled ichthyosis hystrix. As in other ichthyotic dermatoses there may be a familial tendency, or one relative may have a form of ichthyosis while either bullous or nonbullous congenital ichthyosiform erythroderma may develop in another member of the family, as in the case presented.

In the literature concerning ichthyosis and both bullous and nonbullous ichthyosiform erythroderma, the histological attention is not focused on the granular layer

but rather on the horny layer, which is increased and loosely laminated. However, the dyskeratosis mentioned by MacKee and Rosen, previously referred to, is probably not a true dyskeratosis but is in reality a ballooning of the cells of the granular layer. Furthermore, in some of the photomicrographs in MacKee and Rosen's article, the appearance of the granular layer is not unlike that in our case, and this factor substantiates our opinion.

Microscopic evidence suggests that ichthyosiform erythroderma, with or without bullae, ichthyosis, and ichthyosis hystrix are variations of the same disease process. All show involvement of the keratohyaline layer.

As we described, sections show a retiform pattern of the granular layer—ballooning of the cells, clear spaces about the nuclei, and increased size of the granules in these spaces—similar to that seen in ichthyosis hystrix (as represented by the father) and in so-called epidermodysplasia hystricoidis bullosa.

Is It a Combination of Ichthyosis and Epidermolysis Bullosa?—Apparently the bullae are not those of epidermolysis bullosa, for they do not develop instantaneously; they never appear on the mucous membranes; they do not necessarily occur at points of pressure or of trauma; they are never hemorrhagic, and they do not produce scarring. The histopathologic picture is not that of epidermolysis bullosa, even though some reports have recorded a fragmentation of the elastic tissue in bullous congenital ichthyosiform erythroderma.

CONCLUSION

"Congenital keratoses with bullae," "ichthyosis bullosa," and "epidermodysplasia hystricoidis bullosa," are apparently synonyms for bullous congenital ichthyosiform erythroderma. The latter is the same disease as the nonbullous form and in turn is a variant of ichthyosis, as is ichthyosis hystrix. The microscopic change is primarily in the granular layer.

Our careful review of the clinical and microscopic features in the reported cases and of our case suggested many important problems. We believe that a discussion of these problems would be beyond the scope of this article, but we hope that they may form the basis for future investigation. For example, the mechanism of the changes in the granular layer, the possible etiologic factors underlying these changes, the development of the bullous lesions, and the reason for the adverse effect of corticotropin on the bullae, could all be provocative subjects for further study.

ABSTRACT OF DISCUSSION

Dr. Roy L. Kile, Cincinnati: One of the features of this paper by Drs. Barker and Sachs is the clear-cut manner in which they answer some of the questions about this obscure and fortunately rare skin disease. It is difficult for any one person to draw many conclusions regarding a disease that is rare. One large skin clinic has had only two such cases over a 15-year period.

Dr. R. Weiss, in a personal communication, tells me that he feels this congenital abnormality is a variant of ichthyosis vulgaris, or as Pusey once put it, "ichthyosis with erythema." He feels quite sure that it is not nevoid in character. However, there are some definite variations from ichthyosis vulgaris. In some areas of the body, there is an increase in the amount of sweat and sebum in congenital ichthyosiform erythroderma. This is entirely different from their almost complete absence in most cases of ichthyosis vulgaris that I have observed. Histo-

logical examination of the sweat glands apparently varies depending on the area from which they are taken. In this case, some degenerative changes were seen; however, in many reported cases, they have been normal.

I have recently seen two members of a family who have typical ichthyosis with the usual seasonal variations, extensor involvement, and decreased sweating. However, they also have hyperkeratosis of the palms, erythema over the hands, and patchy follicular erythematous lesions over the body that resemble pityriasis rubra pilaris. These intermediate cases help emphasize the relation between the disease under consideration and ichthyosis. When bullae occur, it is harder to continue this relation. I agree with the authors that these bullae are usually not just secondary infections. Of course, in some instances, they may be secondary and not intrinsic, as in the case here presented. This type may possibly be more like those seen in the cases of epidermolysis bullosae reported by Cannon, in which cures in some instances resulted from penicillin therapy.

The positive Nikolsky sign, present only during the period when corticotropin was given, is an interesting observation. Why should this occur? Goldman tells me that in work with the local use of cortisone, the basement membrane of the epidermis stains much lighter with periodic acid-Schiff stain. When the drug is withdrawn, the normal darker stain again is restored. Theoretically, this may account for some physiochemical reason why bullae occur after trauma only during the period of corticotropin therapy. I wonder whether Dr. Barker has any explanation for this? Normally-occurring bullae in his case were in the granular area, however.

The careful histologic study done by the authors is excellent. Their presentation should help all of us to approach this problem more intelligently. This disease is more than just a lack of skin lubrication by sweat or sebum. It is a congenital abnormality of cornification that may or may not have bullae.

By such complete reports as this one, we shall gain a concept of the proper orientation of this disease. Our knowledge is certainly meager at present.

Dr. Ashton L. Welsh, Cincinnati: I want to make one point. I had a patient from a family in which seven members, representing four generations, had this syndrome. Vaccination was performed on three members of the group. Two of the patients were vaccinated while they had bullous eruptions, and in each instance, eczema vaccinatum occurred. In the other patient, vaccination was carried out when the patient was free from bullae, and there was nothing but a normal vaccination reaction. I think it important that vaccination not be done during the bullous episodes of this disease.

Dr. Francis A. Ellis, Baltimore: I have enjoyed Dr. Barker's paper very much, but I wish to go on record as saying that ichthyosiform erythroderma is not a variant of epidermodysplasia verruciformis. In congenital ichthyosiform erythroderma the persistence of the epithrichial cells is rather characteristic. I think that the ballooning of cells accounts for the bullae or the spaces. In the case reported by Dr. Beerman, the vesicle or lacuna had its base just above the basal layer. The balloon cells occur lower than in epidermodysplasia verruciformis. Epidermodysplasia verruciformis usually occurs in Asiatics and is definitely a precancerous disease. The lesions are usually spotty, whereas in most patients with ichthyosiform erythroderma that I have seen the lesions have been plaque-like, more so than in the patient reported on by Dr. Barker.

The granules in the cells and the cells themselves in ichthyosiform erythroderma are usually rather uniform, whereas in epidermodysplasia verruciformis there is more variation in the size of the cells and in the size of the granules. Nor does one see (at least so far as I know) as large areas or groups of these cells in epidermodysplasia verruciformis.

Dr. Louis H. Winer, Beverly Hills, Calif.: I congratulate Dr. Barker on his presentation of this very rare condition. The histologic section showed colliquative degeneration in the granular zone. Microscopically, the father's ichthyosis hystrix also showed changes in the stratum granulosum, in that there was an increase in the number and size of the granules. This increase in keratin precursor accounts for the hyperkeratosis. The large vesicular cells suggest the postfetal retention of the embryonal turgid cells. The bulla is entirely intraepidermal and within the stratum granulosum. This differs from epidermolysis bullosa in which

the site of the blister is subepidermal. We may classify congenital ichthyosiform erythroderma with the epidermal nevi, in which group are the related condition of ichthyosis hystrix, nevus unius lateralis, etc.

DR. HOWARD J. PARKHURST, Toledo, Ohio: It might be of interest to report the progress in a case which I first encountered in 1930 and which was reported at a clinical meeting of this organization in Cleveland in that year. The diagnosis was confirmed at that time by Dr. Otto Foerster. The patient, a boy who was then 6 years old, had a severe generalized involvement and many blisters. I have seen him at intervals since that time, and he has led an active life, including several years of service in the merchant marine. Bland oils and occasionally boric acid ointment have been used, but only irregularly. Through the years his skin condition has gradually improved, and now the ichthyosiform erythroderma has disappeared completely. There have been no blisters during the last four or five years.

DR. LESLIE P. BARKER, New York: I wish to thank those who have taken part in the discussion. I am unable to account for the Nikolsky sign being positive only during corticotropin therapy. There have been no mucous membrane lesions at any time in this patient.

Some patients with this condition have spontaneous improvement; that is, the bullae may cease forming and the erythema disappear, leaving the cutaneous picture of ichthyosis.

In answer to Dr. Ellis, we have not tried to prove a relationship between this disease and epidermodysplasia verruciformis, but merely to point out the fact that the two diseases have similar histologic changes.

MAJOR AND MINOR SURGICAL PROCEDURES ON PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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EAST ST. LOUIS, ILL.

THREE patients with systemic lupus erythematosus who required major operations have recently been observed. The decision to operate was given with some trepidation, in view of the reputed ill effects of surgical trauma in such cases. For example, textbooks state that it is dangerous to attack foci of infection by surgical methods, as this may cause an acute flare-up of lupus erythematosus, with possible death.[1] Review of the literature revealed a difference of opinion as to whether surgical operations had any direct or indirect effect on patients suffering from this disease. Rothman and Felsher [2] state: "Attempts to remove foci or alleged foci in subacute and acute cases have often ended with catastrophic results. The systemically ill lupus erythematodes patient cannot stand such procedures." Harold Orr [3] states that "surgical interference of any sort should be avoided. The extraction of a tooth may cause a serious exacerbation, and so slight an injury as that produced by an intramuscular injection may result in a reaction of the skin at the site of injection." On the other hand, Rose and Pillsbury [4] record three cases of subacute and acute lupus erythematosus in women in which surgical castration benefited the patient. Arthur M. Greene [5] reported the case of a 23-year-old white woman whose bone marrow was positive for the lupus erythematosus phenomenon and whose teeth had all been removed one month before admission to the hospital. Although her temperature had been running from 100 to 102 F., she had gained 10 lb. (4.5 kg.) and her general condition had apparently improved. Horne [6]

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4. Rose, E., and Pillsbury, D. M.: Lupus Erythematosus (Erythematodes) and Ovarian Function: Observations on a Possible Relationship, with Report on 6 Cases, Ann. Int. Med. **21**:1022, 1944.

5. Greene, A. M.: Disseminated Lupus Erythematosus: A Report of 3 Cases of Long Duration, Nebraska M. J. **35**:79, 1950.

6. Horne, S. F.; Curtis, A. C., and Kahn, E. A.: Splanchnicectomy for Hypertension in Lupus Erythematosus and Periarteritis Nodosa, Ann. Int. Med. **32**:1202, 1950.

reported a case of acute disseminated lupus erythematosus in a 42-year-old white woman with hypertension on whom a splanchnicectomy was performed. There was no immediate postoperative effect on the lupus erythematosus. The blood pressure fell, only to rise again in two months, and she finally died of uremia six months later. Ormsby and Montgomery[7] state that if foci of infection are to be removed the operation should be done in a period of quiescence.

REPORT OF CASES

CASE 1.—S. M., a 77-year-old white woman, was first seen on Oct. 5, 1951, at Barnes Hospital. She gave a history of epigastric distress accompanied by a feeling of fullness. She had had flatulence, nausea, and vomiting during the previous 15 years. About one year previous to entry there appeared over the dorsum of her right hand a rash which was treated unsuccessfully with various local medicines. The rash gradually spread to involve the left hand, arms, face, and neck. Localized red raised areas were present, but for the most part the eruption was confluent. During the previous five months the affected areas had been treated with x-rays, and bismuth injections had been given weekly. Physical examination at the time of admission to the hospital revealed an obese white woman with normal temperature, pulse, and respiration. The blood pressure was 190/90. The skin of the face and neck was covered with a rough red scaling and confluent eruption. Some of the areas on the arms were denuded in the center and had a dark periphery with moderate puffy edema. Numerous soft nontender lymph nodes were found in both axillae. A Grade II coarse rumbling apical murmur was present. An enlarged firm and slightly tender liver extended down 3 to 4 cm. below the costal margin. Immediately below the liver was a firm smooth slightly tender mass, interpreted as gall bladder.

Laboratory Data.—The red blood cell count was 4,100,000, with a hemoglobin content of 12 gm. The white blood cell count was 36,000, with a normal differential distribution. The thrombocytes (platelets) were adequate, and the urine was normal. The cardiolipin test was negative. Total protein was 9.6 gm. per 100 cc. (albumin 3.5 gm., globulin 6.1 gm.). The serum lupus erythematosus test was positive on three different occasions. Biopsy of the skin of the right forearm showed a picture consistent with lupus erythematosus. X-rays revealed nonvisualization of the gall bladder.

Course.—The patient was free from fever most of the time. A diagnosis of chronic cholecystitis was made, the patient was operated on Oct. 25, 1951; a cholecystectomy was performed. The postoperative course was stormy, with chills, fever, nausea, and emesis for several days. The skin rash, however, was not accentuated. The patient was discharged, greatly improved, on Nov. 9, 1951. Check-up six months later revealed no change in the lupus erythematosus.

CASE 2.—R. B., a 51-year-old white woman, was first seen at the time of admission to Barnes Hospital, on Sept. 24, 1951. She was a married housewife who had been in good health until 1945, when she noticed over the left cheek a brownish rash which was scaly and pitted. The eruption gradually spread over both cheeks and the bridge of the nose. It seemed to fade at times and to become worse when exposed to sunlight. In 1946 a similar rash was noted over the front of the neck. The patient received weekly injections of bismuth from December, 1946, to 1949, at which time she was found to be anemic and a transfusion was given. Numerous liver, iron, and vitamin injections were given subsequently, without notable benefit. In April and May, 1950, the patient was given blood transfusions, corticotropin, and cortisone. In July weekly transfusions were started and were continued until the time of her admission to Barnes Hospital.

Physical examination revealed a white woman with normal temperature, pulse, respiration, and blood pressure. An erythematous, slightly edematous eruption was present on both cheeks and on the nose, suggestive of an acute disseminated type of lupus erythematosus. Tachycardia and palpable spleen were noted, as well as left upper-abdominal tenderness. There was a Grade II blowing apical systolic murmur.

7. Ormsby, O. S., and Montgomery, A. H.: Diseases of the Skin, Ed. 6, Philadelphia, Lea & Febiger, 1944.

Laboratory Data.—The red blood cell count was 1,450,000, with a hemoglobin content of 4.7 gm. The white blood cell count was 14,450, with a normal differential distribution. The thrombocytes were adequate, and the cell volume was 12.5%. The urinalysis revealed a 4+ reaction for albumin. Determinations of serum proteins showed an albumin content of 3.6 gm., and a globulin content of 4.4 gm. per 100 cc. The serum lupus erythematosus test was positive on two different occasions.

Course in Hospital.—The patient received transfusions at daily intervals. Her temperature was at times as high as 104 F. The red blood cell count was raised by the transfusions, only to fall again. A diagnosis of hemolytic anemia was made, and a splenectomy was done on Oct. 23, 1951. The postoperative course was uneventful, and the patient was discharged on Jan. 1, 1952, with a red blood cell count of 4,300,000, a hemoglobin content of 13.9 gm., a thrombocyte count of 205,000, and a white blood cell count of 7,750. Pathological examination of the spleen and lymph node removed at time of operation showed arterioles with periarterial fibrosis of "onion skin" type. These changes were interpreted as being compatible with systemic lupus erythematosus.

CASE 3.—M. S. entered Barnes Hospital on April 3, 1952, with a history of a rash of two years' duration on the forehead, cheeks, and bridge of the nose. The rash was made worse by exposure to sunlight and was accompanied by low-grade fever and arthralgia. About one month previous to entry her temperature rose to 101.5 F., and acute pain in many joints and an over-

TABLE 1.—*Results of Operative Procedures in Three Reported Cases of Acute Systemic Lupus Erythematosus*

Case	Surgical Procedure	Effect on Lupus Erythematosus
1	Cholecystectomy	Unchanged
2	Splenectomy	Unchanged
3	Tonsillectomy	Unchanged

active heart developed. A serum lupus erythematosus test performed at that time was positive, and a diagnosis of acute systemic lupus erythematosus was made.

Physical examination revealed a 30-year-old white woman, with a mild erythematous eruption on the forehead, cheeks, nose, with some stiffness and limitation of motion in the fingers, ankles, elbows, knees, and shoulders. There was a Grade I apical pulmonary systolic murmur and an elevation of temperature of 1 degree.

Laboratory Data.—There was a slight hypochromic anemia and a white blood cell count of 5,550. A repeat white blood cell count on April 21, 1952, revealed 3,500 cells, and a serum lupus erythematosus test on April 18, 1952, was positive. The Kahn test was positive in a 1:16 dilution. The findings on the rest of the laboratory examinations were essentially normal.

Course in Hospital.—Although the tonsils did not appear to be grossly infected, on April 11, 1952, a tonsillectomy was done, following which there was a transient rise in temperature, which returned to normal within one week. The rash was absent at the time of her discharge, on April 27, 1952, and the patient seemed to be in good condition.

COMMENT

A summary of the three cases reported above is shown in Table 1. The decisions to operate in these three cases were made only after a very careful search through the records of systemic lupus erythematosus cases at Barnes Hospital. Twenty-one cases of the disease in which operation had been done at Barnes Hospital from 1947 to the present time were found. In several of these cases there had been multiple operative procedures. Table 2 shows the type of operations and the results. As seen from the Table, there was no operative mortality in any of the cases.

TABLE 2.—*Effect of Various Minor Surgical Procedures on Acute Systemic Lupus Erythematosus in Cases Observed at Barnes Hospital*

Case	Surgical Procedure	Effect on Lupus Erythematosus
1	Multiple abdominal paracentesis	Improved
2	Cystoscopy with pyelography, pneumoperitoneum, aspiration of sternal marrow	Unchanged
3	Bone marrow aspiration, thoracenteses	Unchanged
4	Bone marrow aspiration	Unchanged
5	Incision and drainage of submaxillary gland	Unchanged
6	Bone marrow aspiration, thoracenteses	Unchanged
7	Multiple thoracenteses	Unchanged
8	Biopsy of axillary lymph node, thoracentesis, cystoscopy with retrograde pyelography	Unchanged
9	Biopsy of lymph node, spinal puncture	Unchanged
10	Bone marrow aspiration, thoracenteses, cystoscopy with ureteral catheterization	Unchanged
11	Teeth extraction, sigmoidoscopy	Unchanged
12	Biopsy of deltoid muscle, cystoscopy with pyelography	Unchanged
13	Lumbar puncture, sternal marrow aspiration	Improved
14	Bone marrow aspiration	Unchanged
15	Biopsy of biceps muscle	Improved
16	Bone marrow aspiration	Improved
17	Biopsy of skin and muscle	Unchanged
18	Bone marrow aspiration	Improved
19	Bone marrow aspiration, biopsy of skin and muscle	Improved
20	Biopsy of skin and muscle	Unchanged
21	Bone marrow aspiration, thoracentesis	Improved

SUMMARY AND CONCLUSIONS

In view of the fact that a total of 24 patients with systemic lupus erythematosus were subjected to various minor and major surgical procedures without any direct or indirect effect on the lupus erythematosus, it is concluded that in the past dermatologists were overcautious concerning indicated surgical operations. It is not advocated, however, that operative procedures be performed without thorough study of each individual patient with systemic lupus erythematosus. Certainly, there should be no hesitation in performing surgical operations that may be lifesaving for the patient. Elective procedures, on the other hand, should be done when the disease is in a period of quiescence.

ONYCHOMYCOSIS DUE TO MICROSPORUM LANOSUM

Report of a Case

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A REVIEW of the medical literature revealed a paucity of information concerning the occurrence of onychomycosis due to the Microsporum genera of fungi. In 1945 Montgomery and Casper [1] listed Microsporum lanosum as the cause of onychomycosis in only 1 of 657 cases involving the finger nails at the New York Skin and Cancer Unit during the period 1935 to 1943. An additional 259 cases of onychomycosis of the toe nails were reported in the same article, but no Microsporum species were involved. No details of the one case reported were given in the text. Lewis and Hopper,[2] in their textbook, make no mention of Microsporum affecting the nails. The same is true of the Sutton and Sutton [3] text. Ormsby and Montgomery,[4] in their text, state, "Tinea unguium [is] normally caused by Trichophyton and Epidermophyton floccosum (rarely Microsporum) and less commonly by Candida (Monilia) albicans." Kittredge [5] reviewed the English literature in 1934 and reported no species or variety of Microsporum had ever been known to cause ringworm of the nails. Many other reports of the fungi causing onychomycosis have been published, but none have listed a Microsporum as the etiologic agent.[6]

This case of onychomycosis due to M. lanosum is reported because of the rarity of the condition and the relative lack of reference to it in the literature.

From the Department of Dermatology (Clarence S. Livingood, M.D., Director) University of Texas School of Medicine.

1. Montgomery, R. M., and Casper, E. A.: Cutaneous Manifestations of the Fungi Causing Dermatophytosis and Onychomycosis, J. A. M. A. **128**:77 (May 12) 1945.

2. Lewis, G. M., and Hopper, M. E.: An Introduction to Medical Mycology, Ed. 3, Chicago, Year Book Publishers, Inc., 1948.

3. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, Ed. 10, St. Louis, C. V. Mosby Company, 1939.

4. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, Ed. 7, Philadelphia, Lea & Febiger, 1948.

5. Kittredge, H. E.: Ringworm of Nails: Consideration of Its Incidence, Anatomic Distribution and Etiology, with Suggestions as to Probable Modus Operandi in Infection and Extension Based upon Review of 312 Reported Cases, and upon Clinical Observation, Urol. & Cutan. Rev. **38**:875 (Dec.) 1934.

6. DuBois, C.: Onychomycosis Not Caused by Trichophyton, Dermatologica **86**:57, 1942. Ghosh, L. M.; Panja, D., and Dey, N. C.: Studies on Ringworm-5, Indian M. Gaz. **83**:215 (May) 1948. Rockwood, E. M.: Study of Fungus Infected Nails, Arch. Dermat. & Syph. **22**: 395 (Sept.) 1930. Whitfield, A.: A Note on Some Unusual Cases of Trichophyton Infection, Lancet **2**:237 (July) 1908. Mcleod, J. M. H.: Diseases of the Skin, Ed. 2, London, H. K. Lewis & Co., Ltd., 1933, p. 373.

REPORT OF CASE

A 26-year-old white married woman came to the office in December, 1951, with a complaint of peeling and splitting of the finger nails of the fourth finger of the right and left hands for the previous six months. The process gradually increased in severity, after the onset, with both nails becoming progressively yellowish and opaque. At the time of the initial examination the fourth finger nails of both hands were opaque and lusterless to approximately the midportion

Fig. 1.—Onychomycosis due to Microsporum lanosum. (Photography by F. W. Schmidt, Director, Department of Medical Photography, John Sealy Hospital, Galveston, Texas.)

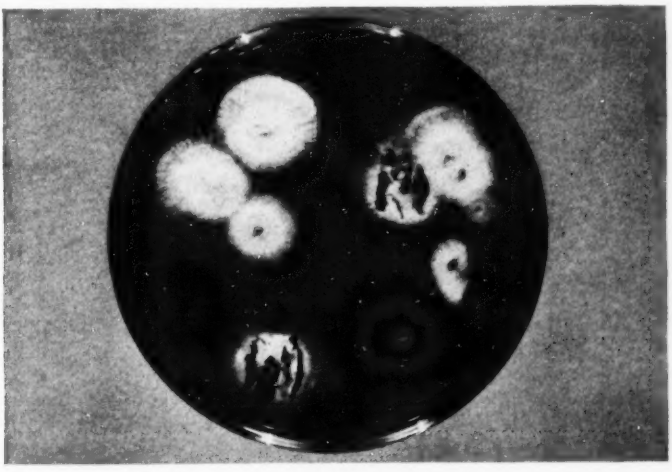

Fig. 2.—Colony growth of Microsporum lanosum on Littman's agar. Black colonies due to saprophytic mold contamination.

of the nail. An inverted yellowish triangular area was present at the lateral surface of each nail with the apex extending toward the nail bed. Figure 1 shows the condition of the nails 17 days after the patient's initial visit to the office.

The nails were scraped with a scalpel into a Petri dish containing Littman's ox bile (oxgall) agar.[7] Within five days, seven discrete colonies of a pathogenic fungus were observed. These colonies are shown in Figure 2. A lactophenol cotton blue mount made directly from this medium revealed the characteristic M. lanosum macroconidia as shown in Figure 3. Transplantation to

7. Littman, M. L.: Growth of Pathogenic Fungi on a New Culture Medium, Am. J. Clin. Path **18**:409 (May) 1948.

Sabouraud's medium resulted in the development of a giant colony characteristic of M. lanosum. Bacterial cultures taken at the same time as the fungus cultures resulted in pure growth of M. lanosum on the blood agar.

The patient was carefully questioned in regard to possible sources of infection. She said that she had had no contact with animals for a period of three months prior to the onset of symptoms. No members of her immediate family had skin lesions which might be interpreted as a superficial fungus infection.

Treatment consisted of the application twice daily of a liquid fungicidal mixture of higher fatty acids, their sodium and copper salts, salicylic acid, and aerosol OT in isopropyl alcohol—a mixture [8] which Capt. Jack W. McNamara, Medical Service Corps, United States Army, Chief of Pharmacy, Walter Reed Hospital, Washington, D. C., and I developed for the treatment of chronic Trichophyton purpureum infections. In brief clinical trials this solution has been shown to be of value in the treatment of T. purpureum infections of the palms and of other parts of the body.

Fig. 3.—Cotton blue mount. Macroconidia of Microsporum lanosum.

This solution was applied to the nail bed after careful scraping and paring. Cultures repeated 17 and 31 days after the start of treatment were negative. Treatment was discontinued after one month. Within another month both nails appeared normal. The patient has remained clinically well for six months.

SUMMARY AND COMMENT

This case was reported because of the rarity of onychomycosis due to the Microsporum genera. The source of the infection was not discovered. Although the response to therapy was prompt in that a complete cure was effected in about eight weeks, no conclusion as to the efficacy of the antifungal agent used can be made because of lack of experience in the treatment of onychomycosis due to the Microsporum genera.

8. Formula consisted of sodium propionate 2%; sodium caprylate 2%; propionic acid 3%; undecylenic acid 5%; salicylic acid 5%; copper undecylenate 0.5%; aerosol OT 0.1%; water, distilled 20%; isopropyl alcohol (91%) sufficient to make 100%.

MYCOSIS FUNGOIDES

Further Report on Cases of Successful Treatment with Antimonials

JOHN GARB, M.D.*
NEW YORK

THIS PAPER is written mainly to reaffirm my belief in the efficacy of the antimonials in some cases of mycosis fungoides. This belief has been strengthened by the continued observation of the 3 out of 10 cases in which there was successful treatment with antimony potassium tartrate U. S. P. (tartar ametic),[1] from personal correspondence, and from results of cases published in this journal.

REPORT OF CASES

Cases 1, 2, and 3 of these aforementioned 10 cases, and that of another patient, W. F. (Case 4), were presented on March 20, 1952, at the Bronx Dermatological Society. Patients 1 and 2 were shown as being completely free of lesions for almost four years following treatment with antimonials, Patient 3 as displaying mild recurrences because of insufficient antimony potassium tartrate injections, and Patient 4 as showing complete involution of the lesions after treatment with lithium antimony thiomalate (Anthiomaline).

CASE 1.—A woman, aged 49, with extensive, generalized tumors and ulcerations of over eight years' duration, responded dramatically to antimony potassium tartrate.[2] She had no recurrences since May 19, 1947, and has been free of lesions since Nov. 29, 1948. The last antimonial (stibophen [Fuadin]) was given on Jan. 13, 1949.

CASE 2.—A woman, aged 52, with generalized infiltrated and nodular growths of six months' duration, likewise showed the dramatic result of antimony potassium tartrate treatment. She had no recurrences since she began to respond to antimony potassium tartrate on Dec. 10, 1947, and has been completely free of lesions since May 9, 1948.

CASE 3.—A man, aged 47, with infiltrated patches and nodular growths of 15 years' duration, responded rapidly to antimony potassium tartrate injections, with only superficial patches remaining. Only 16 injections were given because of myocardial impairment which was present before the treatment was begun. On March 14, 1952, he revealed only mild recurrent lesions, with not much change in his condition after the last injection on Jan. 28, 1948.

Following are cases reported by others in which antimonial therapy was used.

CASE 4 (Patient of Dr. Samuel Fisher).—A woman, aged 51, presented on Nov. 27, 1949, generalized infiltrated patches and fungating growths of two months' duration resistant to x-ray

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* Please note that my name is mispelled Garbe in the discussion of the case of mycosis fungoides presented by Dr. Edward Ringrose, Arch. Dermat. & Syph. **64**:522 (Oct.) 1951.

From the Department of Dermatology and Syphilology of the New York University Postgraduate Medical School (Dr. Marion B. Sulzberger, chairman), and the Skin and Cancer Unit of the New York University Hospital.

1. Garb, J.: Antimony Preparations in the Treatment of Mycosis Fungoides, J. Invest. Dermat. **13**:295 (Nov.) 1949.

2. Please note error in ARCHIVES OF DERMATOLOGY & SYPHILOLOGY **62**:757 (Nov.) 1950, sentence in the second paragraph should read: She received 10 intravenous injections.

exposures. She received intramuscularly 24 injections of lithium antimony thiomalate between Feb. 24 and June 30, 1950. Improvement was noted at about the 15th dose. On September 28 all the lesions had completely regressed, with pigmentation remaining. She had no itching. On Oct. 18, 1950, the patient revealed recurrent scaly and infiltrated patches which subsided after more injections of lithium antimony thiomalate. She was free of lesions from November, 1951, till March 20, 1952, at her last examination.

CASE 5 (Patient of the late Dr. Max Berkovsky [3]).—A man, aged 56, had patches of mycosis fungoides for eight months, which regressed completely after a course of 10 intravenous injections of ethylstibamine (Neostibosan), 0.5 gm., each given once weekly. Two months later a few new lesions developed which disappeared dramatically after one injection of ethylstibamine, with cessation of itching. Unfortunately, because of the death of Dr. Berkovsky the case could not be followed up.

CASE 6 (Patient of Dr. Kemp H. Dowdy [4]).—A man, aged 43, revealed on Aug. 10, 1951, an infiltrating tumor diagnosed as mycosis fungoides d'emblée. He had received no previous therapy. Antimony potassium tartrate, from 1 to 2.5 cc. twice weekly, was given for 15 injections. After the first injection the itching had almost ceased, and after the fourth injection all the lesions had undergone involution.

CASE 7 (Patient of Dr. George M. Lewis).—In discussing a patient of Dr. Andrews [5] who showed a good initial response to antimony potassium tartrate Dr. Lewis stated as follows: "A patient presented at the New York Academy of Medicine two months ago had become roentgen ray fast and was in a critical condition. To our amazement, after only a few doses of antimony potassium tartrate there was involution of all the lesions except for a few small, infiltrated plaques. The response was nothing short of miraculous. Anyone who saw the patient could not help but be impressed with the possibility that this therapy is specific at least in some cases. My associates and I have tried it in 4 cases since, in 1 with good results but in the others with no response."

At the Atlantic Dermatological Conference on March 25, 1950,[6] Dr. Lewis made the following comment about the same patient:

I have followed for several years an 86 year old man with mycosis fungoides who had a spectacular remission after the use of antimony potassium tartrate. This drug may be kept in mind for the treatment of selected cases, and occasionally it will be effective in these very resistant types of lymphoma.

This patient on Feb. 24, 1948, revealed only residual patches after nine antimony potassium tartrate injections in three weeks. Dr. Lewis informed me that this patient died in November, 1950, of the lymphoblastomatous disease with which he had been afflicted.

COMMENT

From the above reports it can be seen that a certain number of patients with mycosis fungoides will respond to antimonials, and two of these patients have been completely free of lesions for about four years. The patients that show regression may do so even after one or two injections of antimony potassium tartrate, and most likely within a period of three weeks. However, in Case 4 response was shown at about the eighth week.

It has been my impression that patients with tumors and ulcerated lesions of long duration react better to antimonials than those in the early stages. However,

3. Berkovsky, M.: Mycosis Fungoides Treated Successfully with Ethylstibamine (Neostibosan®), Arch. Dermat. & Syph. **61**:686 (April) 1950.

4. Dowdy, K.: Personal communication to the author.

5. Lincoln, C. S.: Mycosis Fungoides, Arch. Dermat. & Syph. **61**:342 (Feb.) 1950.

6. Lewis, G. M., in discussion on Roberts, D. P., and Zeligman, I.: Granuloma Fungoides, A. M. A. Arch. Dermat. & Syph. **63**:663 (May) 1951.

Cases 2, 5, and 6, with lesions of six, eight, and two months' duration respectively, show that antimonials may be effective in all stages of mycosis fungoides. Even mycosis fungoides d'emblée, which ordinarily would not be expected to respond to antimony because of the probable lack of sufficient defense by the reticuloendothelial system, deserves a trial with antimonials, as shown by Case 6.

Cases of mycosis fungoides in which there is response to antimony therapy are characterized by early allaying of itching, rapid clearing of the lesions, and, sometimes, by spreading-out of the infiltrated patches, as revealed by Case 2,[7] which appears to be the expression of the reticuloendothelial response in which the skin plays a prominent role.

No conclusions could be drawn as to the percentage of patients benefited by antimonials in the group of 10 cases reported,[1] primarily because it is only a small series in various stages of the disease process, and secondly, since seven of these patients had myocardial and other complications, most of them had to be treated with the much milder antimonials of stibophen and the diethylaminoethanol salt of sodium antimony gluconate (Stibanose). These antimonials do not appear to be very effective in the initial treatment of mycosis fungoides and, certainly, are not as effective as antimony potassium tartrate.

However, even if only 1% of these patients respond, they must be given the opportunity of antimonial treatment before any other is instituted and, surely, after other forms of treatments have failed. For the patient who reacts favorably antimony treatment is not just another palliative measure but appears to act as a specific, as arsenic or penicillin are for syphilis. For that patient the use of antimonials may be a lifesaving procedure which no other treatment has thus far equaled. Even the patient of Dr. Lewis lived two and a half years after the antimony treatment was instituted. Considering his severe illness and advanced age, the addition of two and a half years to his life was a great advance. Furthermore, the antimonial therapy may be repeated for recurrent lesions without causing permanent harm to the system, if careful check-ups of the heart, liver, and kidneys are made regularly.

If the patient responds to antimonials, it is advisable to continue with one to two injections a week of stibophen alone, 5 cc. each or alternating with two injections of the diethylaminoethanol salt of sodium antimony gluconate, 4 cc. each, for six months after all the lesions have undergone regression. This procedure is recommended possibly to prevent recurrences, being similar to the method adopted in the old treatment of granuloma inguinale, said to have prevented recurrences.[8]

If evidence of toxicity develops, as revealed by clinical signs, electrocardiogram, liver-function tests, and urine examinations, the treatment should be suspended for about three to six weeks until the electrocardiogram, the liver-function tests, and the urinalysis show normal results. Liver injections may be continued in the interim. It may be advisable to give liver injections simultaneously with the antimonials as a possible preventive of complications because of the beneficial effect of liver extract on the liver function and its detoxifying ability.[9]

7. Garb,[1] pp., 304-305; Figs. 7 and 8, pp. 300-301.

8. Sobel, N.: Personal communication to the author.

9. Astrachan, G. D.: Crude Liver Extract As Aid to Arseno- and Heavy-Metal Therapy, New York J. Med. **44**:992 (May 1) 1944.

If the patient had myocardial damage, liver disturbance, or kidney damage before treatment was instituted, the question of giving antimonials will have to be decided in each individual case, depending upon the stage of the disease, the degree of pruritus, etc. A patient in the tumor and ulcerative stage, for example, particularly one for whom other treatments have been tried and have failed, should be given courses of stibophen and the diethylaminoethanol salt of sodium antimony gluconate intramuscularly with caution and with intermissions, and a careful watch should be kept on the heart, liver, and kidneys.

It is to be stressed that no less than three injections a week should be given. One or even two injections a week may cause a resistance to antimony and thus deprive the patient of a chance for recovery.

For those patients who complain of nausea and loss of appetite after the administration of antimony potassium tartrate the injection in the evening two hours after a light supper is recommended, allowing them to be rested and strengthened in the morning. Dimenhydrinate (Dramamine) tablets, 50 mg. each, three times daily, will also help to control nausea.

Studies undertaken as to the relationship of the reticuloendothelial system to the response of mycosis fungoides to antimonials, the results of electron microscopic investigations of sections of tissue of mycosis fungoides, and experimental methods of chemotherapy for those patients who do not respond to antimony therapy will be reported as soon as sufficient data have been obtained.

SUMMARY

Cases have been cited to show the effectiveness of antimonials in some patients with mycosis fungoides, with two of these patients completely free of lesions for four years. It has been emphasized that patients with mycosis fungoides should get a trial administration of antimony potassium tartrate (Tartar Emetic) injections for six to eight weeks if there are no contraindications, preferably before any other treatment has been used, and, surely, if other treatments failed. Some cases, even with complications, should have a trial administration of stibophen (Fuadin) alone or alternating with the diethylaminoethanol salt of sodium antimony gluconate (Stibanose) with a careful watch being kept on the heart, liver, and kidneys.

Although the impression has been gained that patients with tumors and ulcerations of long duration responded best to antimonials, cases have been cited in which patients in the early stages and even a patient with mycosis fungoides d'emblée have also responded dramatically to antimonials. For the patients who respond with complete clearing of lesions, antimony treatment is not a palliative method but seems to act as a specific because of the long remissions of about four years in two cases. No less than three injections a week should be given, as infrequent dosage may cause a resistance to antimonials and thus deprive the patient of the only possible chance for recovery. Patients who respond should receive for six months stibophen alone or alternating with the diethylaminoethanol salt of sodium antimony gluconate after all lesions have regressed, possibly to prevent recurrences. For those who feel weak and have loss of appetite following the administration of antimony potassium tartrate the injection should be given two hours after a light supper. Dimenhydrinate (Dramamine) will also help to control the nausea.

ARCHIVES OF DERMATOLOGY

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THE NAME of the second dermatologic journal to appear in the United States was the *Archives of Dermatology*. The first one was the *American Journal of Syphilography and Dermatology*, which was published from January, 1870, to October, 1874, as a quarterly periodical. The first issue of the *Archives of Dermatology* was printed in October, 1874 (the same month as the final issue of the *American Journal of Syphilography and Dermatology*), with L. Duncan Bulkley as editor, and it ceased publication with its number of October, 1882. At its inception the new journal was also a quarterly. There was no connection between the two journals. This is evident from a notice which appeared on page 288 of the April, 1875, issue of the *Archives of Dermatology* under the section "Correspondence and Miscellanies":

> Since the publication of our last issue, a circular has been received announcing the cessation of the American Journal of Syphilography and Dermatology, at the expiration of its fifth year of publication. During the first 2 or 3 years of its appearance it was ably supported by original contributions from our best writers and authorities, but latterly there has been an absolute dearth of original matter, the pages being entirely occupied by reprints and transactions. The editor, giving reasons for its cessation in the circular referred to, says: 'We regret to confess that paltry purposes deprived us of much domestic assistance'. It is indeed unfortunate for one's purposes to be so paltry in the publication of a scientific journal that those to whom he naturally looks for support should fail to give it; it is well, however, to confess, even when too late to mend the error.

The issues of the *Archives of Dermatology* were divided into the following seven sections:

1. Original communications. Most of the articles were by American contributors and almost all of them were on dermatologic (i. e., not urologic) subjects. (In the *American Journal of Syphilography and Dermatology* about half the original articles had been by foreign authors, and many [particularly those which were contributed by American authors] were on urologic topics.)

2. Transactions of the New York Dermatological Society, including papers, cases, and discussions. These transactions were published officially in the journal. The New York Dermatological Society, was not, however, the publisher of the journal.

3. Clinical reports.

From the Department of Dermatology and Syphilology, New York University Post-Graduate Medical School (Dr. Marion B. Sulzberger, Chairman), and the Skin and Cancer Unit of the University Hospital.

4. The digest of literature. This section, according to the editor, contained "a complete summary of everything in periodical literature relating to skin and venereal diseases." Almost all the digests were of foreign articles.

5. Extracts and translations.

6. Reviews and book notices.

7. Correspondence and miscellanies.

During the seventies of the past century not only did the first American dermatologic journals appear, but it was also during this period that the first professional dermatologic associations were founded, the first dermatologic treatises were written, and the first organized didactic instruction in the specialty was given in American medical colleges. All these developments can be followed by reading the *Archives of Dermatology*.

The address of the president at the first meeting of the New York Dermatological Society on May 18, 1869, was printed in the issue of January, 1878. It was called "Dermatology in America," and it was delivered by H. D. Bulkley (father of L. Duncan Bulkley, editor of the *Archives of Dermatology*). It is interesting to note that this address had never appeared in print before. The president called the new organization the "first of its kind in our country."

The July, 1876, issue contained the details of the formation of the American Dermatological Association. The meeting for organization was to be held at the University of Pennsylvania in Philadelphia on Sept. 6, 1876, at the close of the meeting of the section on Dermatology and Syphilology of the International Medical Congress on that day. The notice was contained in a letter signed by L. D. Bulkley, Louis A. Duhring, Lunsford P. Yardell Jr., George Henry Fox, Edward Wigglesworth, and J. E. Atkinzon. The October, 1876, number of the *Archives of Dermatology* had an announcement of the coming "First Regular Annual Meeting" of the American Dermatological Association at Niagara Falls on Sept. 4, 1877. Under "Society Transactions" of the same issue, there was a report of the formation of the organization by Dr. Bulkley, secretary.

The call was sent to about 50 physicians in the various parts of the United States whose names were known in connection with dermatology and suggested by the informal committee issuing the call. Twenty-three gentlemen responded, and these, together with the 6 signers of the call, comprise the 29 original members of the Association. The following officers were elected: President: James C. White (Boston), Vice-Presidents: Louis A. Duhring (Philadelphia) and R. W. Taylor (New York), Secretary: L. Duncan Bulkley, Treasurer: James Nevins Hyde (Chicago). The Association adjourned to meet on the first Tuesday in Sept. 1877 at Niagara Falls.

The January, 1878, issue of the *Archives of Dermatology* printed the president's address, delivered by James C. White at the first annual meeting of the American Dermatological Association, called "Dermatology in America." The October, 1878, number contained the transactions of the second annual meeting of the Association, which was held at Saratoga Springs, N. Y., on Aug. 27 and 28, 1878.

Concerning the establishment of courses for students in dermatology in the curriculum of medical colleges, James C. White, in the president's address at the first annual meeting of the American Dermatological Association, had this to say: "Whereas hardly ten years ago we had not a single officially recognized representative among the great body of medical instructors in the United States, we now have: Professors, 4; clinical professors, 5; instructors, 1; lecturers, 6; total, 16."

The first organized textbooks on dermatology by American authors were Piffard's "An Elementary Treatise on Diseases of the Skin," which appeared in 1876, and Duhring's "A Practical Treatise on Diseases of the Skin," which was published in 1877. Piffard's book was reviewed in the July, 1876, issue of the *Archives of Dermatology*. The October, 1880, issue printed the president's address by Louis A. Duhring at the fourth annual meeting of the American Dermatological Association, in which he said: "In the spring of 1876 was published an elementary treatise on diseases of the skin by Piffard. This was the first strictly original treatise on the subject by an American pen, the book of Worcester being but little more than a compilation, while the several volumes of Damon were monographs only." (Duhring here referred to the book by Noah Worcester called "A Synopsis of Symptoms, Diagnosis & Treatment of the More Common and Important Diseases of the Skin," published in 1845, and Howard F. Damon's "The Neuroses of the Skin: Their Pathology and Treatment" [1868] and "Structural Lesions of the Skin: Their Pathology and Treatment [1869].) Duhring's textbook was reviewed in the April, 1877, issue of the *Archives of Dermatology*; the reviewer (who is unidentified in the periodical) wrote, "We do not hesitate to say that in our opinion this is, in many respects, the best general treatise on diseases of the skin that has ever appeared in any language."

The last number of the *Archives of Dermatology* had the following notice of cessation of publication in the October, 1882, issue:

> With this issue and the completion of Volume Eighth (sic), the Archives of Dermatology will cease its existence. For several years the pressure of other work has rendered it very difficult for the editor to devote sufficient time and energy to its publication and the recent appearance of a monthly journal of cutaneous and venereal diseases has seemed to offer a fit occasion for its discontinuance.

This new periodical was the *Journal of Cutaneous and Venereal Diseases*. In its March, 1883, number there was a reprint of an article which had originally appeared in the *New York Medical Journal* of Jan. 13, 1883, called "Dermatology in America," which told about the disappearance of the *Archives of Dermatology*: "With the number of October 1882, without having shown the slightest sign of decadence, its existence ended, simultaneously with the appearance of a new monthly journal, the Journal of Cutaneous and Venereal Diseases."

30 E. 40th St.

FIRST AMERICAN JOURNAL OF DERMATOLOGY

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NEW YORK

IN EUROPE the development of dermatology as a distinct branch of medicine occurred earlier than it did in the United States. By the middle of the nineteenth century there had already appeared on the continent and in England numerous treatises on skin diseases and at least one periodical (*Les Annales des maladies de la peau et de la syphilis,* 1843, in French). In 1867 *Les Annales de dermatologie et de syphilographie* appeared in French; in 1868 the *Journal of Cutaneous Medicine and Diseases of the Skin* appeared in England under the editorship of Wilson, and the *Archiv für Dermatologie und Syphilis* appeared in 1869 in German; the first and third of these publications have been continued until the present time.

In this country the first journal devoted to dermatology was not published until 1870, and the first organized treatise on the subject was not written until even later. Virtually the only work on dermatology to appear in the United States prior to 1870 was a book by Noah Worcester, which was published in 1845 and called "A Synopsis of the Symptoms, Diagnosis and Treatment of the More Common and Important Diseases of the Skin." Of this book Duhring, in his presidential address called "The Rise of American Dermatology," delivered on Aug. 26, 1879, before the third annual meeting of the American Dermatological Association, said: "The book obviously lacks originality as well as experience, and can therefore scarcely be regarded as more than a compilation from the works of the French and English dermatologists of the day." Against this background of complete foreign domination, it is not surprising to find the pages of the first American dermatologic journal studded with contributions of European authors.

The first journal to appear in this country was a quarterly called *The American Journal of Syphilography and Dermatology,* edited by M. H. Henry, M.D., Surgeon to New York Dispensary, Department of Venereal and Skin Diseases. In the introduction to the first issue, dated January, 1870, the editor noted that "syphilography was designed to comprehend, not merely syphilis, but all diseases, whether general or local, having a venereal origin or lesion." Each issue had a number of "departments," as they were called. The different sections included original communications, reviews, epitomes of current literature, and therapeutic notes. In the second year of publication a department of "clinical contributions" was added; this contained reports of interesting cases, with short remarks. In the third year an item called "About Books" also became a part of the journal. The

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section on original communications was about evenly divided between American and European authors; the others were made up almost exclusively of the contributions of European authorities.

The leading article of the first issue was written by W. Boeck, Professor of Dermatology at Oslo (Christiania), Norway. It was called "On Syphilization," and it discussed the possibility of curing constitutional syphilis by "inoculation with a new primary syphilitic virus." In the last paragraph of the article the author concluded that "my readers will see that I do not believe syphilis is eradicated from the system even by syphilization, but it is forced into a latent state." The first article of the second issue of the journal was "On the Pathology of Eczema" by Foster Swift, Professor of Dermatology in Bellevue Hospital Medical College. The third issue contained a long review by Fredrick Zinsser on "The Doctrines of Unicism and Dualism of the Syphilitic Contagion"; the author discussed "the moot point whether the soft chancre and constitutional syphilis originate in one and the same poison or whether the respective affections are the products of two separate contagions."

The journal contained a number of items of considerable historical interest. In the first issue, the epitome of current literature had an excerpt from the English journal *Journal of Cutaneous Medicine* which read as follows: "Lichen Planus. Under this term Mr. Erasmus Wilson describes an affection which consists in an eruption of papules remarkable for their color, their figure, their structure, their habit of isolated and aggregated development, their local and chronic character, and for the melasmic stains which they leave behind them when they disappear." There followed a good clinical description of the newly described dermatosis, based on 50 cases. The second issue contained a translation of the original description of "On a Peculiar New Formation about the Nose: Rhinoscleroma" by Hebra, of which the original appeared in the *Wiener Medizinische Wochenschrift* in January, 1870. In the October, 1872, issue there was a translation from the *Archiv für Dermatologie und Syphilis* of "Idiopathic Multiple Pigment-Sarcoma of the Skin" by Dr. Kaposi.

The *American Journal of Syphilography and Dermatology* was published for five years. There were twenty issues in all, the final one appearing in October, 1874. In that same month a new periodical called the *Archives of Dermatology* made its appearance. This was a "quarterly journal of skin and venereal diseases" edited by L. Duncan Bulkley. Under "Correspondence and Miscellanies" of the third issue in April, 1875, there was this note:

> Since publication of our last issue a circular has been received announcing the cessation of the American Journal of Syphilography and Dermatology. During the first two or three years its appearance was ably supported by original contributions from our best writers and authorities; but latterly there has been an absolute dearth of original matter, the pages being entirely occupied by reprints and translations.

The *Archives of Dermatology*, which was started independently in October, 1874, appeared as a quarterly for eight years; the final issue was published in October, 1882. In the notice of cessation of publication of the *Archives of Dermatology* (Oct., 1882, vol. 8, no. 4, p. 384) there was no mention of a successor journal:

> With this issue and the completion of Volume Eighth (sic), the Archives of Dermatology will cease its existence. For several years the pressure of other work has rendered it very

difficult for the Editor to devote sufficient time and energy to its publication, and the recent appearance of a monthly journal of cutaneous and venereal diseases has seemed to offer a fit occasion for its discontinuance; the interest of dermatology will be well served by the new monthly, while the Index Medicus furnishes the reference to dermatological literature, which occupied much space in the pages of the Archives.

The *Journal of Cutaneous and Venereal Diseases* made its appearance in October, 1882. In the first number (October, 1882, vol. 1, no. 1) there was nothing to indicate that it was a continuation of a predecessor. The name of this periodical was changed to *Journal of Cutaneous and Genito-Urinary Diseases* in 1887, and again to *Journal of Cutaneous Diseases, Including Syphilis,* in 1903. The final issue, December, 1919 (1919, vol. 37, no. 12), contained the statement that the American Medical Association, at the request of the American Dermatological Association, had taken over the publication of the journal and that it was to be continued as the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY.

It appears evident, therefore, that the predecessor of the present A. M. A. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY is neither the *American Journal of Syphilography and Dermatology* (1870-1874) nor the *Archives of Dermatology* (1874-1882) but the *Journal of Cutaneous and Venereal Diseases.*[1]

30 E. 40th St. (16).

1. This is contrary to the statement made by Pusey: "In January 1870 the American Journal of Syphilography and Dermatology was established with M. H. Henry as editor, and it in turn was succeeded in October, 1882, by the Journal of Cutaneous and Venereal Diseases, with Piffard and Prince A. Morrow as editors, and this journal has continued (under changing names unfortunately) until the present." (Pusey, W. A.: The History of Dermatology, Springfield, Ill., Charles C Thomas, 1933, p. 141.)

CANDIDA ALBICANS

Rapid Identification in Cultures Made Directly from Human Materials

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IN A PREVIOUS paper [1] it was reported that incubation of pure cultures made from thin saline suspensions on Levine eosin-methylene blue agar containing 0.1 mg. of aureomycin per cubic centimeter at 37 C. in 10% CO_2 makes it possible to distinguish Candida albicans from other related species within 18 hours. In the present paper, a similarly rapid identification of this fungus in cultures made directly from samples of human clinical materials is described. The effects of incubating such cultures in air and in CO_2 are compared.

Growth of C. Albicans in Cultures of Materials from Patients with Suspected Moniliasis When Incubated in CO_2 and in Air on Modified Eosin-Methylene Blue Medium

Specimens		CO_2					Air				
		Identification in Days			No Identification*	No Growth*	Identification in Days			No Identification*	No Growth*
Source	No.	1	2	3			1	2	3		
Feces	16	9	7	..	..	..	1	2	..	13	..
Mouth	15	10	4	..	..	1	2	6	..	4	3
Vagina	7	7	..	..	..	..	5	..	..	1	1
Skin	4	3	1	..	..	..	..	3	..	..	1
Nail	8	4	2	1	..	1	..	1	..	3	4
Total	50	33	14	1	0	2	8	12	0	21	9
%	..	66	28	2	..	4	16	24	..	42	18

* "No identification" means that there was growth of yeast colonies, but no filamentation occurred and these colonies could not be identified as C. albicans on the original plate. "No growth" signifies that there was no growth of yeast colonies (that could possibly have been C. albicans) at any time on the plate.

Of the 64 cultures negative for C. albicans on both the CO_2 and air plates, 10 were from feces, 7 from the mouth, 9 from the vagina, 21 from the skin, and 17 from nails.

The 114 specimens used in this study were made from feces, mouth and vaginal secretions, skin, and nail scrapings collected in the clinic from 54 patients with suspected moniliasis or undergoing treatment for or after recovery from proved moniliasis. In many instances materials for culture were taken from several areas of the same patient on the same day. Two samples were taken from each clinical specimen, and these were spread directly over two plates of eosin-methylene blue medium as previously described.[1] Standard size (15 cm.) plates were used for feces and small (5 cm.) plates for the other materials. One of the two plates was

From the Department of Pathology, College of Physicians and Surgeons, Columbia University.

1. Weld, J. T.: Candida Albicans: Rapid Identification in Pure Cultures with CO_2 on Modified E. M. B. Medium, A. M. A. Arch. Dermat. & Syph. **66**:691-694 (Dec.) 1952.

Fig. 1.—Feces. Two days' growth. Feathery colonies of C. albicans interspersed with small round colonies of an unidentified yeast; × 3. Culture grown at 37 C. on modified eosin-methylene blue medium with 10% CO_2.

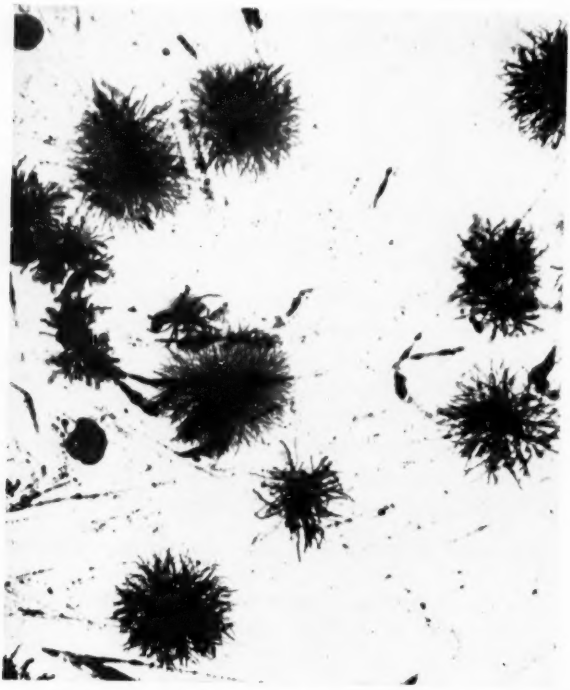

Fig. 2.—Feces. Three days' growth. Several feathery colonies of C. albicans and two smaller bacterial colonies; × 3. Cultures grown at 37 C. on modified eosin-methylene blue medium with 10% CO_2.

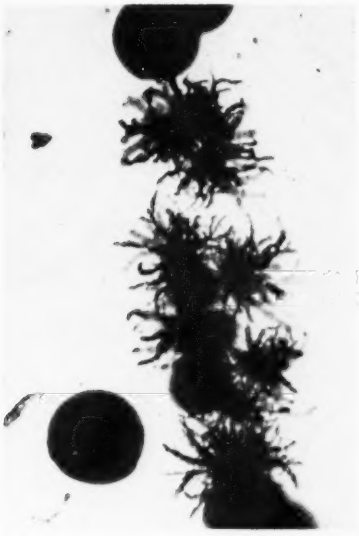

Fig. 3.—Mouth. Two days' growth. Seven colonies of C. albicans and seven round colonies of C. mortifera; × 3. Colonies of C. mortifera have a greenish-metallic luster on the eosin-methylene blue medium. Culture grown at 37 C. on modified eosin-methylene blue medium with 10% CO_2.

Fig. 4.—Skin of palm. Three days' growth. Pure culture of C. albicans; × 6. Culture grown at 37 C. on modified eosin-methylene blue medium with 10% CO_2.

Fig. 5.—Vagina. Two days' growth. Pure culture of spidery colonies of C. albicans; × 6. Culture grown in air.

Fig. 6.—Vagina. Two days' growth. Pure culture of C. albicans; × 6. Culture grown at 37 C. on modified eosin-methylene blue medium with 10% CO_2.

then incubated at 37 C. in air; the other, at the same temperature but in an atmosphere of about 10% CO_2. As a check upon the identification of C. albicans by the eosin-methylene blue-CO_2 method, one colony from every culture so identified was subcultured on Sabouraud's agar and then on corn-meal agar, yielding the characteristic clusters and chlamydospores in every instance. All the strains of C. albicans identified gave the characteristic fermentations for this species. Additional samples were taken in 24 instances and cultured by the usual Sabouraud agar and corn-meal agar method in the department of dermatology, with results agreeing with ours in 20 instances, of which 14 were positive and 6 negative. Of the remaining four specimens cultured, our results were positive for C. albicans and theirs were negative in three instances, and ours was negative and theirs positive in one instance.

From the Table it will be seen that 50 of the 114 specimens proved positive for C. albicans. The Table also shows that the positive cultures incubated in CO_2 were

Fig. 7.—Finger nail. Two days' growth. Pure culture of C. albicans; × 8. Culture grown at 37 C. on modified eosin-methylene blue medium with 10% CO_2.

recognized as C. albicans within one day in 33 of the plates (66%) and within two days in 47 of the plates (94%). There was only one culture in which identification was not made until the third day. In this case the colony when seen on the third day was large and spidery, easily visible to the naked eye. This suggests that it was probably present and should have been recognizable with low magnification on the second day but was overlooked in the routine examination of the plate. All the colonies of C. albicans on the CO_2 plates (48 plates) were characteristically filamentous except in two plates in which an occasional atypical colony was found. In our experience, when C. albicans is grown on modified eosin-methylene blue medium at 37 C., either with or without CO_2, any colony able to put out filaments will do so within two days or not at all. Because this method allows spreading the specimen over an entire plate, a general idea of the number of organisms originally present in a specimen can be obtained by the number of colonies that grow out.

In contrast to the results with CO_2 were those obtained with the cultures incubated in air. In this case 8 cultures (16%) were identifiable within one day, and 20 cultures (40%) within two days. In only 2 of these 20 air-incubated plates were all the colonies filamentous, typical of C. albicans. The other 18 plates contained a scattering of round yeast-like colonies in addition to those showing typical filamentation. In all the instances tested, these round colonies were proved by subculture to be C. albicans. In 21 plates (42%) unidentifiable yeasts developed, showing no filamentation although they were definitely positive when cultured in CO_2. This illustrates the importance of incubating the cultures from human material on the eosin-methylene blue medium with CO_2.

Nine specimens that were yeast-free in air were proved by the incubation of the companion plate in CO_2 to have contained C. albicans. Two specimens were positive for C. albicans in air but not in CO_2. It is felt that these instances illustrate the impossibility of obtaining two uniform portions from a single specimen by random sampling.

SUMMARY

This eosin-methylene blue-carbon dioxide technique for identifying Candida albicans in clinical materials from human patients appears to offer several advantages over the methods now commonly in use:

1. The method is simpler and facilitates following the progress of the disease in patients.

2. The method gives results within two days in contrast to the much longer time required for the usual methods.

3. The method permits estimation of the relative number of C. albicans organisms in a specimen.

Dr. Beatrice M. Kesten, of the Department of Dermatology, obtained the specimens. Dr. Rhoda Benham, of the same Department, assisted with the clinical material used in this study.

TREATMENT OF TINEA CAPITIS WITH SALICYLANILIDE PREPARATIONS

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THE PURPOSE of this paper is to show the relative incidence of the various species of dermatophytes in tinea capitis infections at the Vanderbilt Clinic during the years 1946 to 1949 and to present the results of treating those patients with Microsporum audouini infections with two ointments containing salicylanilide.

At present the treatment of tinea capitis in this country is accomplished almost entirely by one of two methods: (1) the application to the scalp of fungicides combined with manual epilation and (2) epilation of the scalp with roentgen rays followed by the application of local medications and manual epilation of remaining infected hairs. Both methods have their advocates, and often the extent of the infection and the species of fungus recovered determine the method of treatment in the individual patient.

Experience with roentgen epilation shows that this method is safe in the hands of experienced operators. Numerous patients have been treated in this and other clinics during the past three or four decades without a single instance of permanent alopecia. However, permanent alopecia and even radiodermatitis have resulted from x-ray epilation by less experienced persons. Such hazards, therefore, do exist when this type of therapy is infrequently employed. On the other hand, in mass treatment in epidemic cases the pressure of work may lead to carelessness in its application. Aside from the possible dangers, the method is cumbersome and expensive when large numbers of patients are involved.

The ideal local preparation for the treatment of tinea capitis should kill the fungus in the affected hairs without producing undesirable side-effects. However, there is considerable doubt whether any fungicide now available for clinical use accomplishes this feat. Rothman and his co-workers [1] have shown that fatty acid fractions do not penetrate the hair and kill the fungus spores lodged therein.

† Dr. Hopkins died Feb. 27, 1951.

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1. Rothman, S.; Smiljanic, A.; Shapiro, A. L., and Weitkamp, A. W.: Spontaneous Cure of Tinea Capitis in Puberty, J. Invest. Dermat. **8**:81-98 (Feb.) 1947.

Robinson,[2] working with a variety of substances considered "fungicidal," was unable to show that any of them penetrated the hair and killed the spores with the exception of 90% phenol. From these observations, he concluded that the term "fungistatic" was more appropriate than "fungicidal" when referring to these agents. Mitchell,[3] in his discussion of a paper by Swartz and others, expressed the opinion that many compounds widely used for the local treatment of fungous diseases are not really inhibitory. His statement was based on results obtained in a number of in vitro experiments using several popular "fungicidal" preparations. Until such an ideal medicament is found we shall have to consider two other possible effects of chemical treatment, (1) acceleration of the shedding of infected hairs and (2) prevention of spread of infection before the involved hairs are extruded or manually removed.

TABLE 1.—*Distribution of Species of Trichophyton and Microsporum Isolated by Culture from Patients with Tinea Capitis at Vanderbilt Clinic, 1946 to 1949*

Species	No. of Patients	Per Cent
M. audouini	263	80.7
M. canis	56	17.2
T. tonsurans	4	1.2
M. gypseum	3	0.9
Total	326	100.0

TABLE 2.—*Incidence of Kerion in Patients with Tinea Capitis at Vanderbilt Clinic, 1946 to 1949*

Species	No. of Patients	No. Kerions Present Before Treatment	No. Kerions Developing After Treatment	Total No. of Kerions
M. audouini	263	5	18	23
M. canis	56	2	8	10
T. tonsurans	4	1	0	1
M. gypseum	3	1	0	1
Total	326	9	26	35

We reviewed the records of all patients with a diagnosis of tinea capitis seen at the Vanderbilt Clinic during the years 1946 to 1949, inclusive. It is well known that the incidence of the causative organisms varies greatly in various parts of the world, in different sections of this country, and in different periods of time. During the period under consideration 326 cases were proved by isolation of the causative fungus. In 80.1% of these cases the patients were males and in 19.9%, females.

The fungus species identified by culture in these patients are shown in Table 1. The preponderance of M. audouini infections is striking, being 80.7% of the total. This may be due, in part, to a local epidemic.

The distribution of the various organisms according to the sex of the patient did not demonstrate any significant difference.

2. Robinson, H. M., Jr.: In Vitro Studies of Microsporon Audouini Infection of the Hair, Arch. Dermat. & Syph. **57**:991-997 (June) 1948.

3. Mitchell, J. H., in discussion on Swartz, J. H.; Rockwood, F. M., and Glicklich, F. A.: Survey of Tinea Capitis, Including Favus, Arch. Dermat. & Syph. **60**:495-496 (Oct.) 1949.

The incidence of kerion in the group is revealed in Table 2. The figures indicate a rather low incidence of this manifestation, in the light of the experience of most observers. It is possible that some instances were not recorded on the charts. On the other hand, chart entries recording the presence of "inflammation" without further elaboration were not construed to indicate the presence of kerion.

The dermatology department of Vanderbilt Clinic has been engaged for a number of years in the clinical trial of fungicidal compounds. In 1946, Miller, Lowenfish, and Beattie [4] reported on their experience with several treatment agents. The percentage of patients cured of M. audouini infections with use of three of the more promising preparations varied from 9.1 to 12.2%. Of many preparations used more recently, few have given sufficiently encouraging preliminary results to warrant continued investigation. Reports in the literature [5] have indicated the value of ointments containing salicylanilide. We have likewise been encouraged by results obtained with ointments containing this chemical. The analysis of treatment results which follows is based on the use of two ointments with the following formulae:

Ointment SN 1	%
Salicylanilide	5
Benzethonium chloride (Hyamine 1622)	5
Carbowax (polyethylene glycol)	q. s.

Ointment SN 2	%
Zinc undecylenate	25
Undecylenic acid	5
Salicylanilide	5
Carbowax	5

Many of the patients had been used for preliminary trial of new preparations and were given the more reliable salicylanilide ointments only after the trial medicament had failed. Such patients are useless for statistical evaluation, and therefore only those treated from the outset with the ointment in question are included in the tabulations. Our series has been limited to 80 patients with culturally proved tinea capitis caused by M. audouini, whose initial treatment at the clinic was with one of the two ointments described.

The mimeographed instructions given for the management of the case at the time of diagnosis were as follows:

1. Have entire head shaved before your next visit.
2. Wear a stocking cap on the head at all times. This cap is made by cutting the top off an old stocking and tying the cut end in a knot.
3. Wash scalp with soap and water, three soapings, three rinsings, every third day.
4. Thoroughly rub medicine you were given to entire scalp every day.
5. Return to clinic in one week with head washed and shaved and no medicine. Scalp should be clean of all ointment.

A cursory attempt at manual epilation of infected hairs was made at each clinic visit, but usually not more than five minutes a week was devoted to this procedure.

4. Miller, J. L.; Lowenfish, F. P., and Beattie, G. F.: Local Treatment of Tinea Capitis, J. A. M. A. **132**:67-70 (Sept. 14) 1946.

5. (*a*) Schwartz, L.; Peck, S. M.; Botvinick, I.; Leibovitz, A. L., and Frasier, E. S.: Control of Ringworm of Scalp Among School Children in Hagerstown, Md., 1944-1945, J. A. M. A. **132**:58-62 (Sept. 14) 1946. (*b*) Scully, J. P.; Livingood, C. S., and Pillsbury, D. M.: Local Treatment of Tinea Capitis Due to M. Audouini: Importance of Inflammatory Reaction as Index of Curability, J. Invest. Dermat. **10**:111-118 (March) 1948. (*c*) Sullivan, C. N.: Ringworm of the Scalp: Successful Treatment of 7 Institutional Cases by Manual Epilation and Salicylanilide Ointment, Connecticut M. J. **13**:1125-1128 (Dec.) 1949.

Criteria of cure in this study consisted of three negative examinations with Wood's light at intervals of not less than one week, absence of all inflammation, and negative microscopic and cultural examinations.

Tables 3 and 4 present the analysis of the 80 patients. Roentgen ray epilation was employed in some cases because of lack of cooperation on the part of the patient or his family. These cases account for most of those in which treatment was changed. The tables are divided into monthly treatment periods for convenience in establishing the time of cure. The cure rates are calculated by actuarial methods to account for patients who were either lost or changed treatment before the end

TABLE 3.—*Experience of Patients with Tinea Capitis Due to N. Audouini Treated with Ointment at Vanderbilt Clinic, 1946 to 1949*

	Treatment Period, Mo.						
	0-1	1-2	2-3	3-4	4-5	5-6	6-7
No. of patients being treated at beginning of period	36	23	15	10	5	3	2
No. cured in period	0	2	4	2	2	0	1
No. changed treatment during period	6	3	1	3	0	1	0
No. lost to clinic during period*	7	3	0	0	0	0	1
Cure rate in this period†	0	9%	28%	23%	40%	0	66%
Cumulative cure rate‡	0	9%	34%	49%	69%	69%	89%

* Includes one patient in whom Wood's light examination became negative but this patient is not included as cured because of inadequate follow-up.
† Refers to individual monthly period by actuarial methods.
‡ Cure rate obtained by actuarial methods, i. e., expected cure rate if all patients had remained under treatment through that particular monthly period.

TABLE 4.—*Experience of Patients with Tinea Capitis Due to M. Audouini Treated with Ointment 2 at Vanderbilt Clinic, 1946 to 1949*

	Treatment Period, Mo.						
	0-1	1-2	2-3	3-4	4-5	5-6	6-7
No. of patients being treated at beginning of period	44	28	19	6	4	2	0
No. cured in period	1	3	10	1	1	1	..
No. changed treatment during period	9	5	1	0	1	0	..
No. lost to clinic during period*	6	1	2	1	0	1	..
Cure rate in this period†	2.7%	12%	57%	18%	28%	66%	..
Cumulative cure rate‡	0	15%	63%	70%	79%	93%	..

* Includes three patients in whom Wood's light examination became negative but these patients were not included as cured because of inadequate follow-up.
† Refers to individual monthly period by actuarial methods.
‡ Cure rate obtained by actuarial methods, i. e., expected cure rate if all patients had remained under treatment through that particular monthly period.

of the respective periods. A study of these figures suggests that the chance of ultimate cure is near 100% for those patients continuing the treatment, but the patients treated beyond four months are too few to justify such a conclusion. The cumulative cure rates of 34% for ointment 1 and 63% for ointment 2, during the third month, are much more important and significant than the optimistic results shown at six and seven months. The percentage of cures may suggest the superiority of ointment 2 over ointment 1, but the difference is not considered statistically significant. The results with use of both preparations appear considerably better than previously reported results from this clinic. This may be due to superiority of salicylanilide preparations or to greater success in indoctrinating the patients as to thorough treatment.

Of the 36 patients treated with ointment 1, there were 5 with kerion. Kerion had developed in two of these patients before they presented themselves at the clinic. One was cured during the second month of treatment, but the other failed to respond after four months of therapy and was changed to another local medication which brought about cure two months later. Kerion developed in the other three patients after they started using ointment 1. Two of these were lost to the study during the second month of therapy, while the third eventually was cured in the fifth month by use of the drug.

Of the 44 patients treated with ointment 2, 8 had kerion. Only one of these had kerion before treatment but was cured during the third month of therapy with use of this ointment. The other seven patients continued to use the drug, with one patient being lost to the clinic study during the fourth treatment period. The remaining six all went on to eventual recovery using ointment 2, with two cures in the second month, three cures in the third month and one cure during the fifth treatment period.

COMMENT

Our results confirm the observations of others [5] that M. audouini infections of the scalp can be cured in an impressive proportion of cases without resorting to roentgen epilation. Up to the present our best results with local therapy have been obtained by the use of salicylanilide preparations.

We agree with the conclusions of Scully, Livingood, and Pillsbury [5b] that x-ray epilation should be reserved for the three classes of cases defined by them: (1) those in which there is extensive involvement of the scalp with no inflammation, (2) those in which the patient has failed to respond to local therapy after a two- to three-month trial, and (3) those in which cooperation on the part of patient or family cannot be obtained.

In our experience, approximately 60% of all patients with M. audouini infections of the scalp can be cured in two to three months by treatment with an ointment and good hygiene. After this period the cure rate increases slowly. If the Wood light examination is not negative or if there is no marked improvement in the patient by this time, roentgen epilation seems indicated.

It is interesting to note that of the 10 patients adequately followed in whom kerion developed either before or after treatment with salicylanilide, all were eventually cured. This bears out the general impression that patients with inflammatory tinea capitis nearly always recover with local therapy and should not be given roentgen epilation. We should like to point out, however, that the time required for cure of these patients remains about the same as for those with noninflammatory cases of the disease.

SUMMARY

Statistics are presented which show the incidence of culturally identified fungi in 326 patients with tinea capitis at the Vanderbilt Clinic during the period 1946 to 1949.

Experience with the use of two salicylanilide ointments in the treatment of patients with tinea capitis produced by Microsporum audouini is presented.

Dr. J. W. Fertig, Department of Biostatistics, Columbia University of Public Health, assisted in the preparation of the tables.

SIMPLE SCHEME FOR DERIVING X-RAY SKIN-SURFACE DOSE TIMES

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WHEN A superficial x-ray therapy plant is calibrated using a thimble ionization chamber, it is the free-air output of x-rays that is determined. Such free-air doses of x-rays are unsuitable for dermatologic practice, a fact that will be appreciated by contrasting the effect of delivering 100 r in air to areas of different size. If the treated area is the size of a face, back-scatter of x-rays from the body tissues will increase the dose at the surface of the skin to as much as 135 r, whereas delivery of the same air dose to an area of 1 square centimeter may result in a skin-surface dose as low as 101 r. Obviously, the effects on the skin will vary, even though the air dose delivered was the same in each instance.

In order to obtain constant therapeutic effects, all doses given in dermatologic x-ray treatments should therefore be expressed in skin-surface roentgens (r_o).[1] Doses of x-rays delivered must be calculated to allow for back-scatter, so that the x-ray dose on the surface of the skin is not altered by variations in the size and thickness of the region treated and the quality (half-value layer, hardness) of the x-rays used. The system described below enables this to be done with a minimum of time and effort.

It is an established fact that the amount of x-ray back-scatter depends upon the quality of the x-ray beam, the size of the area irradiated, and the thickness of the tissues treated. Back-scatter figures are determined with phantoms of masonite, water, and other substances calculated to absorb and scatter x-rays comparably to human tissue. The actual figures vary somewhat according to the experimental technics employed, but the Commonwealth X-ray and Radium Laboratory provides back-scatter values compiled from the most accurate information available at present.

Graphs were designed from the Laboratory's back-scatter tables to show the number of roentgens in air required to produce 100 r on the surface of the skin for various qualities of x-rays, various field areas, and different thicknesses of tissues. These graphs revealed the percentage of air doses of x-rays which must be delivered in order to produce particular skin-surface doses.[2] The percentages for various treatment factors, as derived from these graphs, are given in the upper part of Table 1. It will be noticed that in the interests of simplicity, treatment

1. The scalp-epilation dose, however, is customarily expressed as a free-air dose.

2. This will be clarified by considering an example. If 95 r in air produce 100 r on the surface of the skin, 95% of the air dose would have to be delivered in order to allow for back-scatter and thus get the requisite skin-surface dose. Accordingly, to obtain the requisite skin-surface dose time, 95% of the air dose time would have to be given.

TABLE 1.—*Back-Scatter Allowance Tables*

	95%	90%	85%	80%	75%	70%
Thick Regions						
Half-value layer 0.6-1 mm. Al.	⊙ 1*-1.75 1-2.5 cm.²	⊙ 2-3.5 3-10 cm.²	⊙ 4-7 12-48 cm.²	⊙ 8-23 50-430 cm.²	⊙ 24-30 450-700 cm.²	....
Half-value layer 1.5 mm. Al.	⊙ 1-1.5 1-2 cm.²	⊙ 1.75-3 2.5-8 cm.²	⊙ 3.5-7 9-38 cm.²	⊙ 8-18 40-260 cm.²	⊙ 19-25 280-500 cm.²	....
Half-layer value 2 mm. Al.	⊙ 1-1.25 1-1.5 cm.²	⊙ 1.5-2.75 2-6 cm.²	⊙ 3-6 7-29 cm.²	⊙ 7-14 30-150 cm.²	⊙ 15-25 100-500 cm.²	....
Half-value layer 3 mm. Al.	⊙ 1-1.25 1-1.5 cm.²	⊙ 1.5-2.75 2-6 cm.²	⊙ 3-6 7-29 cm.²	⊙ 7-10 30-80 cm.²	⊙ 11-22 90-380 cm.²	⊙ 23-25 400-500 cm.²
Thin Regions—Half-Value Layer 0.6-3 Mm. Al						
2 cm. thin						
⊙ 1-1.25	⊙ 1.5-2.75	⊙ 3-8	....	....	....	....
1 cm.²	1.5-6 cm.²	7-50 cm.²	....	....	....	....
1 cm. thin						
⊙ 1-2	⊙ 2.25-5	....	....	....	....	....
1-3 cm.²	4-20 cm.²	....	....	....	....	....
Use Air Dose Times†	95%	90%	85%	80%	75%	70%

Air Dose Times	Skin-Surface Dose Times					
	95%	90%	85%	80%	75%	70%
2 sec.	2 sec.	2 sec.	2 sec.	2 sec.	2 sec.	1 sec.
4 sec.	4 sec.	4 sec.	3 sec.	3 sec.	3 sec.	3 sec.
6 sec.	6 sec.	5 sec.	5 sec.	5 sec.	5 sec.	4 sec.
8 sec.	8 sec.	7 sec.	7 sec.	6 sec.	6 sec.	6 sec.
10 sec.	10 sec.	9 sec.	9 sec.	8 sec.	8 sec.	7 sec.
12 sec.	11 sec.	11 sec.	10 sec.	10 sec.	9 sec.	8 sec.
14 sec.	13 sec.	13 sec.	12 sec.	11 sec.	11 sec.	10 sec.
16 sec.	15 sec.	14 sec.	14 sec.	13 sec.	12 sec.	11 sec.
18 sec.	17 sec.	16 sec.	15 sec.	14 sec.	14 sec.	13 sec.
20 sec.	19 sec.	18 sec.	17 sec.	16 sec.	15 sec.	14 sec.
22 sec.	21 sec.	20 sec.	19 sec.	18 sec.	17 sec.	15 sec.
24 sec.	23 sec.	22 sec.	20 sec.	19 sec.	18 sec.	17 sec.
26 sec.	25 sec.	23 sec.	22 sec.	21 sec.	20 sec.	18 sec.
28 sec.	27 sec.	25 sec.	24 sec.	22 sec.	21 sec.	20 sec.
30 sec.	29 sec.	27 sec.	26 sec.	24 sec.	23 sec.	21 sec.
32 sec.	30 sec.	29 sec.	27 sec.	26 sec.	24 sec.	22 sec.
34 sec.	32 sec.	31 sec.	29 sec.	27 sec.	26 sec.	24 sec.
36 sec.	34 sec.	32 sec.	31 sec.	29 sec.	27 sec.	25 sec.
38 sec.	36 sec.	34 sec.	32 sec.	30 sec.	29 sec.	27 sec.
40 sec.	38 sec.	36 sec.	34 sec.	32 sec.	30 sec.	28 sec.
42 sec.	40 sec.	38 sec.	36 sec.	34 sec.	32 sec.	29 sec.
44 sec.	42 sec.	40 sec.	37 sec.	35 sec.	33 sec.	31 sec.
46 sec.	44 sec.	41 sec.	39 sec.	37 sec.	35 sec.	32 sec.
48 sec.	46 sec.	43 sec.	41 sec.	38 sec.	36 sec.	34 sec.
50 sec.	48 sec.	45 sec.	43 sec.	40 sec.	38 sec.	35 sec.
52 sec.	49 sec.	47 sec.	44 sec.	42 sec.	39 sec.	36 sec.
54 sec.	51 sec.	49 sec.	46 sec.	43 sec.	41 sec.	38 sec.
56 sec.	53 sec.	50 sec.	48 sec.	45 sec.	42 sec.	39 sec.
58 sec.	55 sec.	52 sec.	49 sec.	46 sec.	44 sec.	41 sec.
1 min.	57 sec.	54 sec.	51 sec.	48 sec.	45 sec.	42 sec.
2 min.	1 min. 54 sec.	1 min. 48 sec.	1 min. 42 sec.	1 min. 36 sec.	1 min. 30 sec.	1 min. 24 sec.
3 min.	2 min. 51 sec.	2 min. 42 sec.	2 min. 33 sec.	2 min. 24 sec.	2 min. 15 sec.	2 min. 6 sec.
4 min.	3 min. 48 sec.	3 min. 36 sec.	3 min. 24 sec.	3 min. 12 sec.	3 min.	2 min. 48 sec.
5 min.	4 min. 45 sec.	4 min. 30 sec.	4 min. 15 sec.	4 min.	3 min. 45 sec.	3 min. 30 sec.
6 min.	5 min. 42 sec.	5 min. 24 sec.	5 min. 6 sec.	4 min. 48 sec.	4 min. 30 sec.	4 min. 12 sec.
7 min.	6 min. 39 sec.	6 min. 18 sec.	5 min. 57 sec.	5 min. 36 sec.	5 min. 15 sec.	4 min. 54 sec.
8 min.	7 min. 36 sec.	7 min. 12 sec.	6 min. 48 sec.	6 min. 24 sec.	6 min.	5 min. 36 sec.
9 min.	8 min. 33 sec.	8 min. 6 sec.	7 min. 39 sec.	7 min. 12 sec.	6 min. 45 sec.	6 min. 18 sec.
10 min.	9 min. 30 sec.	9 min.	8 min. 30 sec.	8 min.	7 min. 30 sec.	7 min.

* ⊙ 1 means a circular area 1 cm. in diameter.
† I. e., back-scatter is negligible.

areas are grouped to provide a working accuracy within ± 2.5%, which, taking everything into accout, appears to be well within the range of accuracy ordinarily obtainable in x-ray therapy.

The lower part of Table 1 reduces air dose times to skin-surface dose times, in accordance with the percentages indicated in the upper part of the Table. In actual practice, it is convenient to use a spring-backed folder with the relevant half-value layers out of the upper part of Table 1 pasted across the top, beneath which are sheets showing the times given in the lower part of the Table, one minute on each page,[3] correctly aligned beneath the treatment area columns.

Finally, it is necessary to prepare a chart of air dose times, such as the example in Table 2. These times are calculated from the free-air output of the x-ray plant,[4]

TABLE 2.—*Air Dose Times*

Half-value layer 0.6 mm. Al	Air Dose Times		
Cones	100 r	200 r	1600 r
2/23 cm.	25″	50″	6′39″
3/23 cm.	23″	46″	6′5″
6/23 cm.	22″	45″	6′
15/30 cm. } 22/30 cm. }	41″	1′21″	.....

Half-value layer 1.9 mm. Al	Air Dose Times			
Cones	100 r	200 r	800 r	1000 r
2/23 cm.	1′5″	2′10″	8′42″	10′52″
3/23 cm.	1′	2′	8′	10′
6/23 cm.	59″	1′58″	7′50″	9′48″
15/30 cm. } 22/30 cm. }	1′40″	3′20″	.....	.....

and are the only figures requiring revision after recalibration of the plant. Any number of air dose times can be shown, depending on individual requirements.

The manner of using this scheme will probably be best understood by an example. Suppose that it is desired to give an x-ray treatment with the following data:

Dosage desired = 100 r_o (skin-surface dose)
Half-Value Layer = 0.6 mm. Al
Thick region
Area = circle, 12 cm. diameter
Cone = 15/30 cm.

The determination of the skin-surface dose time is carried out in three steps:

1. The air dose time. Table 2 shows that at half-value layer 0.6 mm. Al, with the 15/30 cm. cone, 100 r (air dose) will be delivered in 41 seconds.

3. Simple additions will give the details for over one minute, for example, 95% of 2 minutes 12 seconds will be 1 minute 54 second + 11 seconds = 2 minutes 5 seconds.

4. If the free-air output is determined to be x roentgens per minute, the calculation of the time for 100 r (air dose) is $\frac{100}{x} \times 60$ seconds.

For 800 r, it would be this figure multiplied by 8.

2. The back-scatter allowance. The upper part of Table 1 shows that at half-value layer 0.6 mm. Al, on a thick region, a circular area 12 cm. in diameter will require delivery of 80% of the air dose time in order to obtain the requisite skin-surface dose time.

3. The skin-surface dose time. The lower part of Table 1 shows that 80% of 41 seconds is 33 seconds.[5] This, then, will be the time required to produce 100 r_o (skin-surface dose) with these treatment factors.

SUMMARY

X-ray doses in dermatologic practice should be expressed in skin-surface roentgens.

A table is provided which enables air dose times to be converted to skin-surface dose times for various x-ray treatment factors.

Using this method, only a few simple calculations are required after each recalibration of an x-ray plant.

Mr. J. F. Richardson, M.Sc., A.Inst.P., of the Commonwealth X-ray and Radium Laboratory, gave his advice in the preparation of this article.

5. In cases such as 95% of 51 seconds, use 48 seconds.

USE OF PODOPHYLLIN (PODOPHYLLUM RESIN) IN DERMATOLOGY

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THE PURGATIVE properties of podophyllum peltatum (May apple root) were known to the American Indian before the time of the white man.[1] Its local use was recommended as early as 1861 for the treatment of "fungus growths," combined with zinc sulfate and hydrastine in the treatment of "cancerous growths," and because of its contrairritative action it was used in "chronic and obstinate cases of local neuralgic pain, spinal irritation, chronic hepatitis, pleuritis, synovitis, morbus coxaruis, etc." [2]

Although Kittredge [3] has stated that the local application of podophyllin podophyllum resin has long been used in New Orleans in the treatment of condylomata acuminata, it was not until the report of Kaplan [4] that this form of therapy became a matter of record. Subsequent reports have firmly established its value.[5]

The treatment of verruca vulgaris has not been so successful.[6] Juvenile warts have occasionally been treated with success,[7] as have plantar warts,[8] although some

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(Footnote continued on next page)

form of maceration must be used in order to make the podophyllin effective. The use of the drug for the treatment of skin carcinoma was reported by Sullivan,[9] in 1949. Other investigators have reported on the treatment of various types of skin cancer with the local application of podophyllin.[10] Larsson [10g] states that squamous cell carcinomas should not be so treated. Wyss-Chodat [10e] agrees. Larsson [10g] and Smith and Garrett [10c] report that this form of therapy is of particular value in areas previously treated by irradiation. Prolonged observation of epitheliomas so treated should be made, as the lesions may recur.[11] Other conditions which have been treated with locally applied podophyllin include the following: molluscum contagiosum,[12] tinea capitis,[13] granuloma inguinale,[14] amyloidosis cutis,[15] acanthosis nigricans,[16] mycosis fungoides,[17] senile keratosis, and other premalignant lesions,[18] ver-

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18. Smith and Garrett.[10c,d] Hall.[10f]

ruca senilis,[19] psoriasis,[5g] weeping eczema,[20] contact dermatitis,[20a, b] and lichen simplex chronicus.[21]

I have used podophyllin with success in the treatment of condylomata acuminata, and, according to the technique outlined by Hall,[10f] in the treatment of keratoses, of superficial epitheliomas, and of recurrent epitheliomas after irradiation therapy. In the present study, my chief interest is in the treatment of recalcitrant dermatoses with very weak concentrations of podophyllin.

The mode of action of podophyllin in weak concentration is not completely understood. Vilanova and Cardenal [22] have found a drying effect when the drug is used in weak concentration. King [23] described mitotic disturbances after the single application of an 0.5% alcoholic solution of podophyllin to the skin of mice. Neither of these explanations seems adequate. Podophyllin locally applied is effective on some dry dermatoses. In a small series of patients treated by me, colchicine and urethan, which have the same effect on cell mitosis as does podophyllin, did not seem to have as much of the therapeutic effect of podophyllin.

The presence of a certain amount of moisture seems to favor the action of podophyllin. It has been shown repeatedly that moist condyloma acuminatum responds to podophyllin while the dry verruca vulgaris does not. The perianal lichen simplex chronicus of one of my patients responded, while a plaque of similar dermatitis on the scrotum was resistant until the strength of the podophyllin dose was increased to 0.2%.

Podophyllin is inactivated in normal solutions of potassium and sodium hydroxide.[24] This fact, however, does not seem to account for the failures recorded, for the perianal is one of the most alkaline areas of the body [25] on which podophyllin has been used in the present study, with the most success. The concentration of the active principles of podophyllin varies in different shipments of the drug,[26] and this variation may account for the difference in reactions reported. While podophyllotoxin was once thought to be the most important active principle in podophyllin, α- and

19. Smith and Garrett.[10c] Hall.[10f]

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24. Sullivan, M., and Blanchard, K.: Podophyllotoxin, Bull. Johns Hopkins Hosp. **81**:65 (July) 1947. (*b*) Sullivan, M.: Podophyllotoxin, Arch. Dermat. & Syph. **60**:1 (July) 1949.

25. Burtenshaw, J. M. L., and MacKenna, R. M. B.: Modern Trends in Dermatology, New York and London, Paul B. Hoeber, Inc., 1948, p. 166.

26. Warren, L. E.: Assay of Resin of Podophyllum, J. A. Official Agric. Chemists **13**:117, 1930; cited by Young.[13c] Vilanova; Cardenal, and Pou.[20b] (*c*) Merck Index, Ed. 6, Rahway, New Jersey, Merck & Co., Inc. 1952, p. 768.

β-peltatin are similarly effective in producing regression of mouse tumors [27] and of condylomata acuminata.[28] The peltatins are related to podophyllotoxin,[29] but appear to be much less irritating.[28]

The reported reactions to podophyllin when locally applied have in the past been a deterrent to its local use. Its irritating properties have frequently been recognized.[30] Reactions from the local application of podophyllin in strengths of 20 to 25% have varied from only an erythema of the surrounding skin, even when the area was covered for 72 hours with adhesive plaster,[7e] to discomfort and pain,[31] particularly when large plaques are treated;[10d] reactions under the prepuce have required circumcision.[5b] In two of Larsson's patients urticaria developed. He noted no other systemic reactions, aside from transient hyperpyrexia, in the treatment of 76 patients with epitheliomas and 18 with precancerous conditions.[10f]

In high concentration, podophyllin is a potent irritant. King and Sullivan [32] found that 30% of 100 men tested with a 25% concentration in liquid petrolatum had positive reactions in 24 hours. Sixty-nine per cent of another similar group had positive reactions in 48 hours. Of 22 positive reactors retested in one to three months, all reacted, 10 with a severer reaction than the original one. In four cases, there was reactivation of the previous test site. Of 23 previously negative reactors, 18 remained negative and 5 became positive.[5e] Sullivan found that of 60 men tested with a 1% and with a 10% solution of podophyllin, and with the same strength of podophyllotoxin, 8% reacted. Vilanova and Cardenal [22] reported that of 20 people with various dermatoses tested with podophyllin in an 0.1% concentration, 5 reacted. The same subjects tested with podophyllotoxin in like concentration showed no reactions. Weaker dilutions caused no positive reactions to either preparation. Subsequently, Vilanova, Cardenal, and Pou [20b] reported on the treatment of 116 wet and exudative types of eczema and contact dermatitis without observing general intoxication or local intolerance. Podophyllin in an 0.1% concentration in zinc paste, sometimes with crude coal tar added, and podophyllotoxin, 0.05% in zinc paste, were used. Reported results were excellent. Retesting the patients a month after treatment did not elicit any positive reactions.

Because of the favorable therapeutic results reported in this country and abroad, further investigation of the therapeutic possibilities of podophyllin seemed indicated.

27. Greenspan, E. M.; Leiter, J., and Shear, M. J.: Action of Peltatins on Lymphomas and Other Tumors in Mice, Cancer Res. **9**:597 (Oct.) 1949. Leiter, J.; Downing, V.; Hartwell, J. L., and Shear, M. J.: The Action of Substances Extracted from Podophyllin on Sarcoma 37 in Mice, ibid.

28. Sullivan, M., and Hearin, J. T.: Treatment of Condyloma Acuminatum with Peltatins, to be published.

29. Hartwell, J. L., and Detty, W. E.: Isolation, Properties and Chemistry of Alpha- and Beta-Peltatins, Cancer Res. **9**:597 (Oct.) 1949.

30. (*a*) Bentley, R.: Podophyllum Peltatum, Pharm. J. **3**:456, 1861. (*b*) O'Donovan, W. J.: Dermatitis Due to Podophyllum Resin, Brit. J. Dermat. **47**:13, 1935. (*c*) Morrow, P. A.: Selected Monographs on Dermatology, 1893, p. 521. (*d*) Ransom, cited by Bentley,[30a] p. 463. (*e*) Winterburn, G. A.: Eruption from Podophyllin, Louisville, M. News **8**:187, 1877. (*f*) Webster, D.: A Case of Poisoning by Contact of the Powder of Resin of Podophyllum, M. Rec. **12**:357, 1877.

31. Lain, E. S., in discussion on Smith and Garrett.[10d]

32. King, L. S., and Sullivan, M.: Effects of Podophyllin and of Colchicine on Normal Skin, on Condyloma Acuminatum and on Verruca Vulgaris, Arch. Path. **43**:374 (April) 1947.

The patients treated in this series had, for the most part, become resistant to conventional therapy or had failed to respond. Many of them had been given all the irradiation which they could safely tolerate. A strength of 0.1% was selected and was used for the most part throughout the present study. On the glabrous skin, zinc oxide ointment USP was the usual vehicle. On the scalp, 91% isopropyl alcohol with 2% castor oil added was used. The patients were instructed to apply the medication themselves; no patients were treated in the office. The alcoholic solution was applied to the scalp or the occipital region either with a medicine dropper or with a cotton applicator. The ointment was applied with the fingers. Strict instructions were given to avoid getting medication in contact with the eyes,

TABLE 1.—*Results of Treatment*

	Objective Improvement				Subjective Improvement					
Diagnosis	Marked	Moderate	None	Worse	Marked	Moderate	None	Worse	Patch Test Patients Made Worse	Total Patients
Lichen simplex chronicus	14*	7	4	1	21*	1	3	1†	Negative	26
Nuchal eczema	9	1	0	0	9	1	0	0	.....	10
Perianal perivulvar pruritus	0	0	0	1‡	5	0	0	1‡	Negative	6
Psoriasis	11	13	6	1	10	1	5	1	Not done	31
Dermatitis venenata, hands (lichenified)	9	0	0	1	9	0	0	1	Negative	10
Nummular eczema	2	5	3	0	4	4	1	1§	Negative	8
Stasis dermatitis	1	1	1	1	1	1	1	1	Negative	4
Exudative dermatitis, hands ‖	1	3	4	2	1	2	5	2	1 Positive 1 Negative	10
Miscellaneous¶	2	2	10	2#	3	1	7	2#	2 Positive	16
Total	49	32	28	9	63	11	22	10		123

* In one patient with a perivulvar eruption asymptomatic aphthous-like ulcerations of the vaginal mucosa developed. The ulcerations cleared when treatment was discontinued and did not recur when treatment was resumed, with more care used in the application of the medication.

† Patient improved and then relapsed.

‡ Irritation of mucous membrane of protruding hemorrhoidal tags developed.

§ After treatment to control exudation, the patient tolerated podophyllin ointment without irritation.

‖ This includes patients with atopic eczema, with dyshidrotic eczema, and with unclassified exudative eruptions of the hands.

¶ One patient with keratoderma climactericum, one with a pustular bacterid, one with dermatitis herpetiformis, three with psoriaform seborrhea, two with flexural atopic eczema, one with exudative dermatitis of the legs and ankles, and two with proved Microsporum purpureum infections were treated without success. One patient with an unidentified superficial mycotic infection (proved by positive scrapings) had moderate improvement. He was not cured. In one patient with slightly lichenified neurodermatitis there was complete control of the pruritus and moderate improvement in the eruption while treatment was being applied; in another patient with a similar condition no relief was obtained. The treated areas of a patchy slightly scaling erythematous dermatitis due to vitamin A were controlled, as was one case of seborrheal otitis externa. A single plaque of lichen planus disappeared after two months' treatment; the pruritus was controlled immediately. Another patient with lichen planus became worse after ten days' treatment.

One patient has lichen planus and one has exudative dermatitis of the legs and ankles.

because of the danger of conjunctivitis. When used near the anus or vulva, instructions were given to avoid the mucous membranes for fear of irritation. A feeling of "soreness" was complained of by several patients in the course of therapy. This "soreness" did not appear to be a true reaction, but was rather an irritation from the too frequent or too generous application of the medication. The complaint was largely eliminated by instructing the patients to apply the medication only every three days at first and then gradually to increase the frequency of application, if complete control of the pruritus was not obtained, and if the medication was tolerated. Rarely was it desirable to apply the medication more often than once daily, and often a satisfactory therapeutic result was accomplished when the applications were made only every two or three days. It was sometimes necessary to continue application every few days to maintain a clinically satisfactory condition. Table 1 summarizes the results of treatment.

COMMENT

The effect of podophyllin on pruritus was frequently remarkable. The difficulty of evaluating the effect of any method of treatment upon pruritus is appreciated.[33] Since many of the patients treated had previously failed to respond to treatment either from me or from other physicians, it is felt that they more or less served as their own controls. In most of the psoriatic patients, only single areas were treated, leaving the other areas as controls. More extensive controlled work such as that of Garb [21] would be desirable.

The control of pruritus was not always followed by objective improvement, and when objective improvement did occur, it was usually rather late in the course of treatment. One patient with lichen simplex chronicus of an ankle had little objective improvement, although the pruritus subsided and did not recur over a 2-month period of observation, even though no further therapy was applied.

In my series, podophyllin was particularly effective in relieving pruritic conditions of the perianal and perivulvar areas (Table 2). Pruritus ani et vulvae as used in this paper refers only to conditions in which there was no clinical evidence of dermatitis other than as the result of excoriation. The results of treat-

TABLE 2.—*Results of Treatment of Conditions Involving Interglutcal and Perivulvar Areas*

Diagnosis	Objective Improvement				Subjective Improvement				Patch Test Patients Made Worse	Total Patients
	Marked	Moderate	None	Worse	Marked	Moderate	None	Worse		
Psoriasis	4	1	1	0	5	0	1	0	.....	6
Lichen simplex chronicus	9*	1	1	1	11	0	0	1†	Negative	12
Pruritis ani vulvae	5	0	0	1‡	5	0	0	1‡	Negative	6
Total	18	2	2	2	21	0	1	2		24

For explanation of symbols see Table 1.

ment of nuchal eczema (suboccipital dermatitis) were excellent. In lichenified contact dermatitis of the hands, the drug was very useful. Eight out of nine patients had marked improvement; in the ninth vesiculation developed, although the patch test with the ointment gave a negative result. In contact dermatitis as in neurodermatitis, environment has much to do with continued improvement; reexposure to irritating factors causes relapse. Although patients with nummular eczema, when in its vesicular phase, were sometimes relieved, patients with wet or oozing dermatoses did not, in general, show much improvement. Failure was encountered in most cases of exudative dermatitis of the hands. Stasis dermatitis did not respond in a satisfactory manner, although exudation had ceased before the podophyllin ointment was applied.

There were 11 unfavorable reactions to treatment. Three patients (one with lichen planus, one with exudative dermatitis of the legs and ankles, and one with exudative dermatitis of the hands) reacted to the medication with true allergic sensitization, as manifested by a positive reaction to the patch test. Patch tests on the other patients showing unfavorable reactions to treatment (aside from the one psoriatic who was not tested) gave negative results. Results of simultaneous tests with the vehicle were, in all the patients tested, negative. In two patients reactions

33. Corson, E. F.; Luscombe, H. A., and Decker, H. B.: Experience with a New Antipruritic Agent, A. M. A. Arch. Dermat. & Syph. **65**:187 (Feb.) 1952.

developed which were probably the result of irritation of the mucous membrane rather than of the skin. The vaginal mucosa of one patient developed asymptomatic aphthous-like ulcerations. The ulcerations healed when treatment was stopped and did not recur when treatment was resumed, with more care given to the application of the ointment. The other patient, who had pruritus ani with hemorrhoidal tags, experienced a severe recurrence of his pruritus and irritation of the hemorrhoidal tags. A patient with lichen simplex chronicus of the perineum improved temporarily, but then became worse with continued therapy. One patient with nummular eczema complained of severe burning for 12 hours after the first application of the ointment. Later, when exudation was controlled, he was able to tolerate the medication without difficulty. In addition to the patients mentioned above, one patient with contact dermatitis of the hands, one with exudative dermatitis of the hands, one with stasis dermatitis, and one with psoriasis did not tolerate treatment. It is probable that the incidence of unfavorable reactions could have been lowered had no exudative conditions been treated, or if treatment with podophyllin had been withheld until other therapy had controlled the exudation. More care in the application of the ointment around the anal and vaginal orifices would likewise have lowered the incidence of reactions. No lesions on the face were treated, because of the danger of conjunctivitis. Regardless of precautions, it is unlikely that the incidence of true allergic sensitization would be lowered; in fact, if the use of podophyllin is extended, the incidence of allergic sensitization may be expected to increase.

SUMMARY AND CONCLUSIONS

One hundred twenty-three patients suffering from various types of dermatitis were treated with locally applied podophyllin; the results of treatment are reviewed. The local application of podophyllin is very useful in the treatment of lichen simplex chronicus, nuchal eczema, and pruritus ani et vulvae. It is also helpful in the treatment of localized areas of psoriasis (particularly perianal and perivulvar), lichenified contact dermatitis of the hands, and occasionally in nummular eczema. Of the other conditions treated, either the number of patients treated was too small to gain even an impression of results, or the treatment was a failure.

The incidence of unfavorable reactions to treatment was relatively high (11 out of 123 patients). Podophyllin is particularly irritative when used adjacent to the mucous membrane. No patients with dermatitis of the face were treated, because of the danger of conjunctivitis.

ABSTRACT OF DISCUSSION

Dr. Leslie M. Smith, El Paso, Texas: Podophyllin is a valuable drug in dermatology and has many possible uses. It will take a great deal of clinical experimentation with various concentrations and various derivatives of podophyllin before we can feel sure just what the drug will do and what it will not. Dr. Nelson's attempt at evaluating the drug has been honest and careful and will serve as a basis for further work.

My own work with podophyllin has been, until recently, confined to the stronger concentrations of the drug. I have recently been using it as 0.1% paste as suggested by Dr. Nelson. I have been greatly impressed with both its efficacy and its ability to cause irritation and soreness in such a weak concentration. It has been especially useful in pruritus ani, and by applying it only once every two or three days and a milder antipruritic between times I have been able to control some cases in which there had been failure to respond to any other therapy. The same applies to lichen simplex chronicus. Daily applications can usually not be continued for a long time without reaction or the development of the characteristic soreness which Dr. Nelson mentioned.

Podophyllin must be kept away from the eyes, and anyone who doubts the need of this caution can easily be convinced by a single experience with a severe and persistent conjunctivitis due to this drug.

Podophyllin can also be occasionally used to advantage in 5 or 10% suspensions in compound benzoin tincture in certain chronic thickened lesions such as psoriasis and lichen simplex, but this treatment should be made an office procedure on account of the danger of reaction.

Several years ago Sullivan in Baltimore, and Garrett and I in El Paso, working independently, found that certain keratoses and basal cell epitheliomas could be made to disappear with the use of 20 to 25% suspensions of the drug. Fletcher Hall confirmed the effect on keratoses, and some other investigators are now finding that it can be used usefully in basal cell epithelioma, although there have been two unfavorable reports. Podophyllin is seldom the method one would choose in treating the average epithelioma, on account of the difficulty of determining when the lesion is sufficiently treated.

We have had a number of patients with recurrences who had to be treated again, but we also have a large number of patients who have remained well for over three years. The method has virtue and should not be forgotten, though it is not for routine use. Neither is it for haphazard use, and careful attention to the details of technique must be observed. We do use podophyllin almost routinely in our office in the treatment of multiple superficial basal cell epitheliomatosis, a relatively benign and superficial condition. This condition can be handled with this drug with much less scarring than with other methods and the lesions can be just as surely cured, if one is careful to observe the points of technique necessary, such as removal of all necrotic tissue before each application.

In the further investigations on podophyllin, derivatives of the drug will undoubtedly receive the most attention. If the peltatins retain all the beneficial properties of podophyllin without being the irritant that popophyllin is, as the recent work of Sullivan and his co-workers indicates, podophyllin should be a very useful and popular drug in our dermatologic formulary.

VITAMIN D_2 IN TREATMENT OF NONTUBERCULOUS CHRONIC SKIN DISEASES

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THIS STUDY was stimulated by Dr. Gustav Riehl, whose world-famous lupus hospital in Vienna I visited in the summer of 1950 and again in 1951. Subsequently, I undertook to translate, edit, and revise his book, "Skin Tuberculosis and Its Therapy."[1] I was impressed by the dramatic results obtained with vitamin D_2 therapy in skin tuberculosis, a condition heretofore resistant to all types of treatment save prolonged heliotherapy. Charpy,[2] the most outstanding pioneer in vitamin D_2 therapy, called it "a sunbath in an ampule." This description, although an oversimplified one, led me to investigate its value in skin conditions which were known to be definitely benefited by the action of sunlight.

HISTORICAL REVIEW

The healing action of the sun, so essential to all parts of life, has been recognized intuitively by mankind since the early ages. It took, however, some time until concrete proof of its importance was demonstrated. It was Palm,[3] in 1890, who demonstrated the connection between rickets and the lack of sunshine. It was also known for some time that lupus vulgaris occurred most frequently in countries with little sunshine, long before its tuberculous origin was established. In the 90's of the last century Finsen [4] introduced, in his native Denmark, irradiation with carbon-arc-light, under compression, as a substitute for sunlight. In Switzerland famous mountain sanatoriums were built at the beginning of this century, thanks to the initiative of Bernhard and Rollier,[5] primarily for the treatment of bone tuberculo-

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1. Riehl, G., and Köpf, O.: Die Hauttuberkulose und ihre Therapie, Wilhelm Maudrich, Vienna, 1950.

2. Charpy, M. J.: Le traitement des tuberculoses cutanées par la vitamine D_2 à hautes doses, Ann. dermat. et syph. **6**:310, 1946.

3. Palm, T. A.: The Geographical Distribution and Ætiology of Rickets, Practitioner **45**:270, 1890.

4. Finsen, N. R.: Natürliche Sonne: Das Kohlenbogenlicht, in Handbuch der Haut- und Geschlechtskrankheiten, edited by J. Jadassohn, Vol. 10, Pt. 1, Volk, R.: Tuberkulose der Haut: Lupus erythematodes, Granuloma annulare, edited by F. Veiel and F. Jacobi, Berlin, Springer-Verlag, 1930, p. 879.

5. Bernhard, and Rollier, A.: Heliotherapie, in Handbuch der Haut- und Geschlechtskrankheiten, edited by J. Jadassohn, Vol. 10, Pt. 1, Volk, R.: Tuberkulose der Haut: Lupus erythematodes, Granuloma annulare, edited by F. Veiel and F. Jacobi, Berlin, Springer-Verlag, 1930, pp. 443, 444, and 446.

sis, but also for lupus, where the use of sunlight, which is particularly rich in ultraviolet rays in high altitudes, was utilized in the form of general irradiation. Only after progress was made in the development of vitamin research was it recognized that the most important healing action of sun or ultraviolet rays is due to the synthesis of vitamin D in the skin, brought about by the irradiation of sterols. Ultraviolet-irradiated cholesterol is, as we know today, vitamin D_3, while vitamin D_2 is irradiated ergosterol, which is found in plants. In 1919 Huldschinsky [6] healed rickets by using ultraviolet light; later, Hess [7] and Steenbock [8] proved that ultraviolet-irradiated food possesses an antirachitic action; therefore there must be present in the food a provitamin which, under the influence of light, can be transformed into the active substance. Hess,[9] Pohl,[10] and Windaus [11] demonstrated that the provitamins are sterols, of which ergosterol is the most potent. The synthesis of irradiated ergosterol was accomplished by Windaus [12] in 1926 and was marketed under the name of Vigantol by Merck & Company, Inc.

On the other hand, the Scandinavians probably have known for some time that cod liver oil has a distinct healing action on certain diseases. Darbey [13] treated bone afflictions and rheumatism, as well as lupus, in Manchester, England, in 1766, with large doses of cod liver oil. In 1830, Trousseau [14] in Paris and, a few years later, Bazin [15] used cod liver oil in treating tuberculous conditions. In his lectures in the 1850's, Hebra [16] praised cod liver oil therapy for lupus. Soon thereafter this therapy was abandoned, since high amounts were obviously not well tolerated by the patients and low amounts were not efficacious.

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6. Huldschinsky: Allgemeinbelichtungen, Natürliche Sonne, in Handbuch der Haut- und Geschlechtskrankheiten, edited by J. Jadassohn, Vol. 10, Pt. 1, Volk, R.: Tuberkulose der Haut: Lupus erythematodes, Granuloma annulare, edited by F. Veiel, and F. Jacobi, Berlin, Springer-Verlag, 1930, pp. 518, and 527; Heilung der Rachtitis durch künstliche Höhensonne, Deutsch. med. Wchnschr. **45**:712, 1919.

7. Hess, A. F.: The Antirachitic Activation of Foods and of Cholesterol by Ultraviolet Irradiation, J. A. M. A. **84**:1910, 1925.

8. Steenbock, H., and Daniels, A. L.: Irradiated Foods and Irradiated Organic Compounds, J. A. M. A. **84**:1093, 1925.

9. Hess, A. F., and Windaus, A.: Experiments on Activation of Cholesterol by Ultra-Violet Irradiation, Proc. Soc. Exper. Biol. & Med. **24**:171, 1926; Contaminating Substances as Factor in Activation of Cholesterol by Irradiation, ibid. **24**:369, 1927; Development of Marked Activity in Ergosterol Following Ultra-Violet Irradiation, ibid. **24**:461, 1927.

10. Pohl, R.: Über das Absorptionspektrum des antirachtisch-wirksamen Cholesterins, Nachr. Ges. Wiss. Göttingen, math.-physik. Klasse, p. 1942, 1926; ibid. p. 185, 1926.

11. Windaus, A. and Holtz: Die experimentelle Rattenrachitis und ihre Beziehung zum Ergosterin, Nachr. Ges. Wiss. Göttingen, math.-physik. Klasse, No. 2, p. 217, 1927.

12. Windaus, A., and Hess, A. J.: Sterine und antirachtisches Vitamin, Nachr. Ges. Wiss. Göttingen, math.-physik. Klasse, p. 175, 1926.

13. Darbey, cited by Charpy.[2]

14. Trousseau, A.: Clinique médical de l'Hôtel-Dieu de Paris, Ed. 2, Paris, Baillière, 1865.

15. Bazin, E.: Die Behandlung der Hauttuberkulose: Nichtspezifische Allgemeinbehandlung (Lebertran), in Handbuch der Haut- und Geschlechtskrankheiten, edited by J. Jadassohn, Vol. 10, Pt. 1, Volk, R.: Tuberkulose der Haut: Lupus erythematodes, Granuloma annulare, edited by F. Veiel and F. Jacobi, Berlin, Springer-Verlag, p. 453, 1930.

16. Hebra, F.: Demonstration eines hypertrophischen exulcerierten Lupus vulgaris, ausschliesslich mit Lebertran geheilt, Ges. Ärzte in Wien **8**:80, 1851.

In 1922 Hopkins and MacCollum [17] and their co-workers isolated two fat-soluble vitamins from cod liver oil. One was the heat-resistant antirachitic-acting vitamin D, and the other was vitamin A. The synthetically manufactured vitamin D, unfortunately, contained a large amount of highly toxic substances which were formed after extensive irradiation and were later recognized as toxisterol, suprasterol, etc. The aforementioned experiments of Hess [7] and Steenbock [8] led finally to the manufacture of a pure product by photochemical means from irradiated ergosterol, the vitamin D_2 of Windaus.[18] Bourdillon,[19] in England in 1931, independently produced a substance which he called calciferol.

Charpy [2] described the rationale which led him to try this new method:

> The leading concept was very simple and naive and originated from the well-known fact that general heliotherapy in lupus, according to the technique of Rollier,[5] was for some time considered a classic in Switzerland. In these patients who were in the institution for treatment, consisting of prolonged exposure of their naked bodies to sunlight, it appeared as a logical assumption that the favorable, often decisive, action which was observed in the isolated tuberculous areas of the skin, although they themselves were carefully covered, was due to the transformation of ergosterols [!] in the skin into vitamin D. The functioning of the extensive "skin factory" of about 1 square meter surface for several hours daily could only lead to the formation of considerable amounts of vitamin D. . . . Would it not be possible to obtain the same results, much more simply, by giving the same patients the pure vitamin D in high doses which was apparently responsible for the healing? The only reservation was a priori that this procedure had to be free of danger, and that it was not to lead to a severe disturbance of the calcium metabolism.

This started a new era in the therapy of skin tuberculosis.

CHEMISTRY AND BIOLOGIC ACTION OF VITAMIN D_2

The chemical formula of vitamin D has been known since 1931 (Windaus,[18] Bourdillon [19]). It is an isomer of ergosterol, $C_{28}H_{44}O$. The synthesis of vitamin D_2 has so far been unsuccessful. It is not, as some believe, only irradiated ergosterol. It is an intermediary product of this photochemical procedure. During the process other transformation products are formed at the same time, such as lumisterol, tachysterol, toxisterol, suprasterol I and II, of which some are especially toxic or have calcifying action. It has to be separated from these. The correct technique of separation by means of crystallization was only started in 1931-1932, and only since 1933-1934 have pure chemical products been available. Vitamin D_2 is crystalline, insoluble in water, but soluble in ether, 90% alcohol, acetone, and oil. The solvent, according to Charpy,[2] plays a role. The different action in various countries can probably be traced to this fact.

Absorption via the intestinal tract is complete provided a normal bile function exists or with concomitant administration of bile salts. The oily solutions are equally well absorbed when given parenterally. In every case, regardless of the mode of administration, the intact liver function is a prerequisite to total utilization.

In spite of the numerous investigations in this field, the biologic action of vitamin D_2 is as yet not fully understood. Szent-Györgyi [20] stated in 1937: "The function

17. Hopkins, and MacCollum: Cited by Charpy.[2]

18. Windaus, A.: The Chemistry of Irradiated Ergosterol, Proc. Roy. Soc. London, s.B **108**:568, 1931; Über bestrahltes Ergosterin, Ann. Chem. **489**:266, 1931.

19. Bourdillon, cited by Charpy.[2]

20. Szent-Györgyi: Propriétes physiques et thérapie des vitamins, Congrés de Ch. Solvay, p. 65, 1938.

of vitamin D is unknown and changes in phosphorus and calcium metabolism are only symptoms, which by no means explain the true cellular action; that is the molecular mechanism of its action." Today we have not progressed any further, and we can only say that these actions on the metabolism were studied. The action of vitamin D_2 in the phosphorus-calcium metabolism is very complex and little understood. It varies according to the dose. On the other hand, identical doses have brought about individually different actions, depending on age, endocrine balance, nutrition, phosphorus and calcium intake, digestion factors, mode of living, physical activity, and psychic irritations (Charpy [2]). In spite of all investigations, which have been primarily conducted in the experimental sphere, the mechanism is still a dark and nebulous subject. It appears that vitamin D is not a chemotherapeutic in the ordinary sense, but rather a catalyst and accelerator of a normal process. In the meantime, let those who are satisfied that the advantage of this drug exceeds its danger use it with the precautions which have been recommended from the clinical, pathological, and chemical standpoint.

DOSAGE AND TOXIC REACTIONS

The dosage of vitamin D_2 has been established in the extensive investigations upon skin tuberculosis and varies greatly, depending upon the investigator, but it seems to be agreed upon by all that for adults, a daily dose of up to 200,000 units, given for a considerable time, is safe. The average dose given by most physicians clinically is 50,000 units, three times daily. Children are given a smaller dose depending upon their age.

An extensive pulmonary process, hypertension, kidney disease, chronic intestinal disease, as well as any serious pathologic condition of chronic nature, constitutes a contraindication to its use. Old age as such is considered by Riehl [1] a contraindication. Pregnancy, on the other hand, with the exception of the last few weeks ante partum, and youth are not considered a contraindication.

It is imperative to watch out for an increase in the blood calcium level and to check the kidney function regularly when high doses are being given over a long period of time. Signs of intolerance are to be considered danger signals and, when observed, necessitate the discontinuation of therapy. Intolerance is manifested either in clinical symptoms or in laboratory findings. The first symptom is anorexia, followed by nausea and vomiting. Epigastric distress is considered by many authors as the initial symptom of intolerance. Polydipsia, pollakiuria, and constipation preceding diarrhea are often observed. Disturbances of the nervous system, such as peripheral neuritis and polyneuritis, as well as damage to the optic nerve leading to atrophy, have been observed sporadically. Severe depressive symptoms are sometimes encountered, as well as stuporous conditions in children. In cases of severe toxicity, elevation of the temperature, as well as leukocytosis, does occur. Rost [21] remarked that a drop of leucocyte index is a danger sign of overdosage. Debré and co-workers [22] were able to collect 10 cases in 1946

21. Rost, in discussion on Hartung: Klinische Erfahrungen bei der Behandlung von Hauttuberkulosen mit dem Chemotherapeutikum Tb I 698E. (Domagk), Bericht u. d. gemeins. Tagg. d. Nordwestdeutschen u. Hamburger Derm. Ges.—4.4.1948, v. 2.

22. Debré, R.; Thieffry, S.; Brissaud, E., and Trellu, L.: Les troubles morbides déterminés par la vitamin D_2 administrée à doses trop fortes chez l'enfant, Presse méd. **54**:769, 1946.

in which the patients died after vitamin D therapy. Kalkoff [23] and Langer,[24] as well as Riehl,[1] warned against office therapy with this vitamin by general practitioners.

Of the 108 patients treated with vitamin D_2, untoward reactions were observed in 5. In all five patients the symptoms were rapidly controlled when administration of the drug was stopped and did not recur when it was repeated at a lower maintenance level.

MATERIAL AND RESULTS

A total of 108 patients were treated with vitamin D_2 from July, 1950, until July, 1952. All patients were office patients. Their ages ranged from 2 to 56 years. The sex distribution was about equal. Calciferol (Drisdol [Winthrop-Stearns, Inc.]) given orally, was used throughout the study.

Atopic Dermatitis.—Fanielle [25] reported excellent results in the treatment of asthma and allergic eczemas (atopic dermatitis) as early as 1944. Riehl [1] treated 22 patients with neurodermatitis chronica which had been present since early childhood. In four of these the lesions were healed, and the rest were considerably improved. Relapses were, however, observed in all cases. Goldberg and Dexter [26] treated 20 patients with atopic dermatitis with calciferol. Fifteen of these patients were considerably improved, while five failed to respond to treatment.

Fifty-seven patients with atopic dermatitis were treated by me. Thirty-two had previously been treated by me and by others without much success; 25 patients were new to me but had had all types of therapy most of their lives. I routinely gave 50,000 units daily to children up to 7 years of age, 100,000 units daily to children up to 12 years of age, and 150,000 units daily to all other patients. Never did I give more than 200,000 units daily. The amounts were increased or decreased proportionately to the response of the patients. Blood calcium, phosphorus, and urea nitrogen studies were made at the beginning of the therapy and once a month during the course of treatment. Urine examinations were made weekly.

Of the 57 patients, 15 failed to respond. In three mild albuminuria developed, necessitating the discontinuation of calciferol for a few weeks. Two of the three had mild toxic reactions, such as nausea and abdominal distress. After a few weeks all three were able to tolerate calciferol at a lower dosage and were benefited by it.

Forty-two patients stated that they noted a distinct diminution of itching and a decrease of erythema, as well as a thickness of the involved skin areas within three to four weeks of treatment. These patients were by no means cured, but they improved so much that they were able to pursue a normal life.

The treatment was discontinued by mutual agreement whenever the patients were free of pruritus and the skin was clear except for residual lichenification. Of the 42 patients, 12 remained symptom-free after the therapy was discontinued, most of them for 20 months. Twenty patients relapsed within three to five months after the vitamin intake was withdrawn.

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23. Kalkoff, K. W.: Die Hauttuberkulose im Rahmen der Gesamttuberkulose, Med. Klin. **17**:42, 1947.

24. Langer, E.: Vigantolbehandlung des Lupus vulgaris, Arch. Dermat. u. Syph. **187**:126, 1948.

25. Fanielle, G.: Le D-Vitaminotherapie à doses massives et rapprochées, Liège, 1944.

26. Goldberg, L. C., and Dexter, H. L. T.: Treatment of Chronic Cutaneous Problems with Calciferol, A. M. A. Arch. Dermat. & Syph. **63**:729, 1951.

In order to determine whether the whole effect could be credited to the vitamin intake and was not a psychic one, 15 patients were again given vitamin D_2 in the amounts last used by the individual, but the other 15 received a placebo. It was very interesting to observe that all those who received vitamin D_2 were again controlled within a few weeks, while only two of the placebo group reported subjective improvement, without any objective improvement of the skin. It was also interesting that in the summer months as little as 50,000 units daily was sufficient to control the condition, while as soon as fall came the amount had to be increased to 150,000 units.

Psoriasis Vulgaris.—Ceder and Zon,[27] as well as Huriez and Leborgne,[28] observed an interesting response in psoriasis which, however, rarely led to a cure. Charpy [2] himself saw no uniform results. Kindler [29] treated 31 persons having psoriasis, mostly women and children, with moderate doses of calciferol. Twelve of these patients responded with complete or almost complete recovery while on treatment with daily doses of 50,000 to 100,000 units of calciferol for a period of several weeks to six months' duration. Of the remaining 19 patients, 7 improved. Goldberg and Dexter [26] treated nine persons with psoriasis with calciferol. Five of these patients had generalized psoriasis, and four had focal psoriasis vulgaris. The average dosage of calciferol was 15 drops three times a day. In five of these patients there was improvement during the first three months of treatment; thereafter, relapses occurred in three of these five patients, and further treatment with the drug was discontinued. Two of the patients not only improved under calciferol treatment but continued to improve after treatment was stopped. Four patients failed to show any degree of response. Pascher [30] stated that of 27 patients with psoriasis vulgaris treated with calciferol, 1 patient was cured, 4 showed good improvement, 3 fair improvement, and the remainder no improvement.

Thirty-one patients with psoriasis vulgaris were treated by me with calciferol. Seven of these patients had generalized psoriasis, and the rest showed various stages and involvements of the condition. The disease was present from 4 months to 16 years. The average dosage of calciferol was 50,000 units three times daily. Of the seven patients with generalized psoriasis, two recovered completely within 3 months of therapy and have remained so for 18 months. Three patients showed good improvement, which has remained stationary for the past year, and 2 patients showed no response at all. Of the 24 patients with various degrees of psoriasis, only 5 recovered and remained so for 14 months, 9 showed considerable improvement, while the remaining 10 patients failed to respond.

Acne Conglobata.—Three patients with extensive acne conglobata who previously had been treated unsuccessfully with x-rays were given calciferol, 50,000 units, four times daily. A pronounced improvement was observed within three months, at which time the dosage was reduced to 150,000 units daily, and later to 100,000 units, and they have been given this dose for a year now, with a very gratifying response.

27. Ceder, E. T., and Zon, L.: Treatment of Psoriasis with Massive Doses of Crystalline Vitamin D and Irradiated Ergosterol, Pub. Health Rep. **52**:1580, 1937.

28. Huriez, C., and Leborgne, J.: Psoriasis et vitamin D, Paris méd. **133**:53, 1946.

29. Kindler, T.: Psoriasis Treated with Calciferol, Brit. J. Dermat. **61**:329, 1949.

30. Pascher, F.; Silverberg, M. G.; Marks, I. E., and Markel, J.: Calciferol (D_2), J. Invest. Dermat. **13**:89, 1949.

Lichen Planus.—Clément-Simon [31] reported excellent results in this stubborn condition with vitamin D in oil ("sterogyl") in a remarkably short time. Charpy [2] was able to confirm this in eight cases. Bureau [32] also reported favorable results. Riehl [1] saw a distinct, although not too prompt, healing of a lichen ruber verrucosis.

Eleven patients with more or less generalized lichen planus were treated with calciferol. Five patients were originally given weekly injections of bismuth, alternating with mercury. Six were given only calciferol, 50,000 units three times daily. Both groups were so treated for three months, and the response in both was very slow, to say the least. I then combined the calciferol therapy with heavy metal injections and rapid involution occurred. I can offer no explanation for this response.

Granuloma Annulare.—Like Hall,[33] Pascher,[30] and Riehl,[1] I observed the dissemination of the lesions in three patients. In one patient a quite extensive granuloma annulare developed during the course of the calciferol therapy which was given for his atopic dermatitis.

Keloids.—Charpy [2] reported the rather paradoxical, yet distinct action, of vitamin D_2 on certain keloids. Riehl [1] saw the hypertrophic scars of an old lupus wound become softer and flatter. I have tried this type of therapy on three patients with keloid, without any visible effect.

SUMMARY AND CONCLUSIONS

The effect of vitamin D_2, calciferol (Drisdol) on atopic dermatitis, psoriasis vulgaris, acne conglobata, lichen planus, granuloma annulare, and keloids was investigated in 108 patients over a period of two years. The drug can safely be taken by all age groups for a relatively long period of time, provided the proper safeguards are observed. The historic development and the chemistry and biologic action of vitamin D_2 have been reviewed.

The results attained in atopic dermatitis were very encouraging. Forty-two out of 57 patients with atopic dermatitis definitely benefited from the use of vitamin D_2 in high doses. The improvement became evident within three to four weeks of therapy with this drug. None have been cured. The treatment should be abandoned if there is no response within three to four months. It appears that this drug might be a very valuable adjuvant in the management of this, therapeutically so troublesome, condition.

The results in the treatment of psoriasis were encouraging enough to warrant further study on a large group of patients; the same study should be done in acne conglobata and lichen planus, since a definite favorable response was observed in these conditions. The drug appears to be of no value in treatment of granuloma annulare and keloids.

207 Republic Building.

31. Clément-Simon: Un traitement interne héroique de lupus tuberculeux (le traitement de Charpy), Bull. méd., Paris **26**:369, 1945.

32. Bureau, Y., and Barrière: Résultats obtenus par la vitamine D_2 (Méthode de Charpy) dans le traitement de la tuberculose cutanée et de certaines dermatoses, Ann. dermat. et syph. **5**:196, 1945.

33. Hall, F.: Granuloma Annulare, with Dissemination Following Calciferol Therapy, Arch. Dermat. & Syph. **61**:145, 1950.

HAIRY TONGUE

Report of a Case Following the Use of Aureomycin Ointment

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THE HAIRY tongue is a benign disease entity of somewhat bizarre nature. Characterized by an overgrowth of the epidermis of the filiform papillae, particularly in the triangular area anterior to the circumvallate papillae, the filamentous proliferation produces an appearance which has been likened to "the hair of a dog dampened by water." The color is frequently black, but shades of brown, yellow, blue, and green have been described.

In most instances the condition is asymptomatic, the patient complaining only of the appearance of the tongue. In some cases, however, a sickening taste and pain have been described as occurring in the introspective person. Certain patients have been annoyed by tickling sensations or gagging produced by the elongated papillae.

There has been considerable controversy over the etiology of hairy tongue. Heidingsfeld,[1] in 1910, reviewed the various theories propounded since Raynaud, in 1869, observed hyphae and spores in the filamentous growths. Raynaud's exposition of a parasitic causation spurred others to investigation along this line. Some confirmed his observations, but others failed to do so. Later, other microorganisms were discovered in association with this condition, including a filiform bacillus, round spores, a "black fungus," a peculiar Cladothrix (Actinomyces), Saccharomyces linguae pilosae, and a previously undescribed organism, Oospora lingualis. Heidingsfeld also cited Levisseur, who attributed the condition to the use of silver nitrate and chromic acid; Schnabel and Schourp, who believed that the disorder was a common one among syphilitics, dyspeptics, and tobacco users, and Vollmer, who was of the opinion that syphilis, mercurialization, strong disinfectants, and tobacco were predisposing factors. Heidingsfeld divided hairy tongue into two general classes, true cases and false cases. The former, characterized by persistence and longer filaments, he believed due to some hereditary anomaly of development, while the false cases, which were evanescent and showed shorter filaments, he believed due to local and general irritating and infectious causes, such as tobacco, antiseptics, astringents, and syphilis.

In the years following Heidingsfeld's publication additional reports on hairy tongue were divided between those ascribing to it a parasitic origin and those which maintained that it was a nonparasitic, irritative phenomenon. Weidman,[2] in 1928,

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1. Heidingsfeld, M. L.: Hairy or Black Tongue, J. A. M. A. **55**:2117 (Dec. 17) 1910.

2. Weidman, F. D.: The Affinities Between Black Tongue and Trichomycosis, Arch. Dermat. & Syph. **18**:647 (Nov.) 1928.

cultured a Nocardia from a hairy tongue. Thompson and Montgomery,[3] one year later, isolated a species of Actinomyces from two cases. Swinburne [4] reported on 16 cases of hairy tongue and concluded that the condition was the result of an inflammatory state brought about by various irritants. Kennedy and Howles [5] cultured Candida albicans from two of their three patients. Kleinert [6] isolated Bacillus anthracoides, bacterioides, and alpha-hemolytic streptococci from scrapings of the hairy filaments. Laskaris and Curtis [7] studied three cases of hairy tongue. From this study and their review of the previously reported cases they concluded that there is a fairly consistent type of microflora associated with hairy tongue, namely lactobacilli, micrococci, streptococci, and Candida albicans. It was their belief that these organisms which have supplanted the normal tongue flora, as a result of their acid-producing fermentative activities, provide a continuous chemical irritation. However, they maintained that the role played by these organisms was secondary rather than primary.

After the introduction of antibiotic therapy, reports concerning the development of hairy tongue following these medications began to appear in the medical literature. Bedford,[8] in 1946, reported two cases of hairy tongue following the use of penicillin lozenges. Wolfson [9] reported on four patients with hairy tongue which occurred after the use of penicillin troches or aerosol penicillin. In one of these, Candida was cultured from the tongue scrapings. Woods and co-workers [10] reported on 20 patients with moniliasis of the oropharynx which followed penicillin, aureomycin, or chloramphenicol therapy. They suggested that the overgrowth of Candida was due to suppression by the antibiotic of the competing normal bacterial flora. Harris [11] observed the occurrence of black hairy tongue in 2 out of 110 patients under treatment with oral aureomycin or chloramphenicol. Downing [12] reported a case of black hairy tongue which appeared following the ingestion of 50 capsules of aureomycin (50 mg. each). Phillips [13] observed two cases which occurred following the use of aureomycin troches and one case which occurred after the use of crystalline aureomycin. Tomaszewski [14] noted the appearance of black hairy tongue in 4 out of

3. Thompson, L., and Montgomery, H.: An Organism Isolated from 2 Cases of "Hairy Tongue," J. A. M. A. **93**:114 (July 13) 1929.

4. Swinburne, G.: Black Hairy Tongue, J. Laryng. & Otol. **54**:386 (July) 1939.

5. Kennedy, C. B., and Howles, J. K.: Black Hairy Tongue: A Report of 3 Cases, Arch. Dermat. & Syph. **42**:566 (Oct.) 1940.

6. Kleinert, M. N.: Hairy or Black Tongue, Ann. Otol. Rhin. & Laryng. **55**:188 (March) 1946.

7. Laskaris, T., and Curtis, G. D.: Concerning the "Parasitic" Etiology of Hairy Tongue, J. Invest. Dermat. **13**:99 (Aug.) 1949.

8. Bedford, P. D.: Black Tongue and Oral Penicillin, Brit. M. J. **2**:63 (July 13) 1946.

9. Wolfson, S. A.: Black Hairy Tongue Associated with Penicillin Therapy, J. A. M. A. **140**:1206 (Aug. 13) 1949.

10. Woods, J. W.; Manning, I. H., Jr., and Patterson, C. N.: Monilial Infections Complicating the Therapeutic Use of Antibiotics, J. A. M. A. **145**:207 (Jan. 27) 1951.

11. Harris, H. J.: Aureomycin and Chloramphenicol in Brucellosis, with Special Reference to Side Effects, J. A. M. A. **142**:161 (Jan. 21) 1950.

12. Downing, J. G.: Black Tongue as a Result of Antibiotic Therapy: Report of a Case, New England J. Med. **242**:1013 (June 29) 1950.

13. Phillips, E.: Black Tongue from Aureomycin, J. A. M. A. **143**:1514 (Aug. 26) 1950.

14. Tomaszewski, T.: Side-Effects of Chloramphenicol and Aureomycin, with Special Reference to Oral Lesions, Brit. M. J. **1**:388 (Feb. 24) 1951.

126 patients receiving aureomycin or chloramphenicol capsules. He did microscopic studies on the tongue scrapings of these patients and observed a disappearance of the normal bacterial flora a few days after the start of treatment, with a concomitant increase in fungi such as Candida albicans. The occurrence of black tongue after the taking of terramycin was recently reported.[15] The role played by nicotinamide deficiency induced by antibiotic therapy has been stressed by Ellinger and Shattock.[16]

REPORT OF CASE

G. W., a 52-year-old white man, began the application of aureomycin ointment over the vermilion portion of the lower lip in March, 1952. It had been prescribed to aid in the healing of an area of superficial crusting in the center of the lip which had previously been subjected to a V-excision for squamous cell carcinoma. Shortly after use of the ointment was started the

Brownish-black mass of hair-like processes on dorsum of tongue.

patient noticed that the entire dorsum of the tongue became black. Despite this, he continued to apply the ointment to the lip three times a day. On May 13, he became aware of a growth on the posterior part of the tongue and, because of this, discontinued application of the ointment. During the following week the black color disappeared from all the tongue, with the exception of that in the new growth, which remained unchanged.

When seen on May 20, he said that he had not used mouth washes, astringents, or medications other than the aureomycin ointment. He stated that he smoked less than one package of cigarettes a day. There had been no symptoms, except for an occasional tickling sensation in the throat, which he attributed to the growth on the tongue. Examination revealed a brownish-black elevated mass in the center of the dorsum of the tongue extending anteriorly from the triangle formed by the circumvallate papillae (Figure). The mass was made up of dark hair-like processes which arose from a lighter, whitish area. It was considered typical of hairy tongue.

15. Brackish Taste, Black Tongue, and Antibiotics, Queries and Minor Notes, J. A. M. A. **149**:622 (June 7) 1952.

16. Ellinger, P., and Shattock, F. M.: Nicotinamide Deficiency After Oral Administration of Penicillin, Brit. M. J. **2**:611 (Oct. 26) 1946.

Most of the tumor was curetted off, and a 2% aqueous solution of methylrosaniline chloride (gentian violet) was applied to the area. Direct microscopic examination of some of the curettings in potassium hydroxide failed to reveal fungi. However, a planting on Sabouraud's medium produced a growth of Candida. The patient was instructed to apply the solution of methylrosaniline chloride to the tongue twice a day, and when he was seen two weeks later there was no evidence of hairy tongue. He was examined periodically during the following two months, and there has been no recurrence despite the use of various other ointments, including bacitracin ointment, on the lip.

COMMENT

The development of hairy tongue following the use of aureomycin capsules and troches has been reported often enough to make it, although not common, by no means a rarity. However, to the best of our knowledge, this is the first report of a case in which hairy tongue developed after the application of aureomycin ointment.

Although one may question whether aureomycin was actually the responsible agent, the evidence available would suggest such a cause-and-effect relationship. There was no other obvious cause, the patient disclaiming the use of mouth washes, astringents, and irritants and stating that he was only a light smoker. The pigmentation of the tongue developed shortly after the applications of aureomycin ointment were started and disappeared from most of the tongue after use of the ointment was discontinued. The patient admitted that he frequently licked the lower lip, thereby transferring some of the ointment to his tongue. These events tend to implicate aureomycin as the initiating agent.

The mode of action is not quite so clear. As has been proposed by previous authors, it is possible that the antibiotic suppressed the normal bacterial flora, thereby allowing multiplication of other micro-organisms, such as Candida. The isolation of this fungus and the response to fungicidal therapy suggest that this organism may have played some role in development of the hairy tongue.

SUMMARY

The theories concerning the etiology and nature of hairy tongue are reviewed, and a case of hairy tongue due to application of aureomycin to the lip is reported.

170 Waterman St. (6).

247 Waterman St. (6)

HOTCHKISS-McMANUS STAIN VERSUS CLEARING IN KOH IN THE DIAGNOSIS OF SUPERFICIAL MYCOSES

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IN A RECENT publication Kligman, Pillsbury, and Mescon reported on the superiority of the basic fuchsin staining technique (Hotchkiss-McManus stain) over the traditional potassium hydroxide clearing method in the diagnosis of ringworm infections and moniliasis.[1] They examined 186 patients with dermatoses which clinically suggested fungous infections of the glabrous skin, the feet, and the nails. The KOH specimens revealed the presence of fungi in 48 cases, or 25.8%, while the staining method showed fungi in 60 cases, or 32.3%, of the 186 cases in which examination was made.

Two essential steps are involved in the Hotchkiss-McManus staining procedure. First, the polysaccharides present in the cell walls of fungi are transformed into polyaldehydes by means of periodic acid. Second, a deep red color develops in the areas containing such aldehydes in the presence of leucofuchsin (Schiff aldehyde reagent), so that the fungous elements will stand out sharply against a pale pink or colorless background.

PURPOSE, MATERIAL, AND PROCEDURE

In order to investigate the relative value of the Hotchkiss-McManus stain as compared with the conventional KOH method, we examined 340 patients with dermatoses clinically suggesting superficial fungous infections in the mycology section of the Skin and Cancer Unit of the New York University Hospital. The conditions examined included dermatophytosis of the hands and the feet, tinea corporis and tinea cruris, onychomycosis, moniliasis (paronychial and intertriginous form), tinea versicolor, and six cases of suspected tinea capitis which did not fluoresce under Wood's light.

Scrapings from the skin or the nails and hairs from the scalp were taken in the usual way. One portion of the material was cleared and examined in potassium hydroxide, another was stained, and, except in cases of tinea versicolor, a third portion was cultured on Sabouraud's medium.

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1. Kligman, A. M.; Pillsbury, D. M., and Mescon, H.: Improved Technic for Diagnosing Ringworm Infections and Moniliasis, J. A. M. A. **146**:1563, 1951.

Our staining method followed, with slight modifications, the technique described by Pillsbury and Kligman.[2] The scales or hairs were placed on a slide covered with a film of an albumen-glycerin mixture and left to dry for a few hours at room temperature, so that the material adhered firmly to the slide. The slides were then treated in the following manner:

1. Immersed in 95% alcohol for two minutes.
2. Immersed in a 5% aqueous solution of periodic acid (crystalline periodic acid may be obtained from G. Frederick Smith Chemical Co., Columbus, Ohio), for seven minutes.
3. Rinsed in tap water for two minutes.
4. Stained in Schiff reagent for seven minutes.
5. Rinsed in tap water for two minutes.
6. Dehydrated through 95% alcohol for two minutes.
7. Dehydrated through absolute alcohol for two minutes.
8. Dehydrated through xylene for two minutes.
9. Mounted in Harleco synthetic resin or other mounting fluid.

Results of Three Diagnostic Methods in 200 Cases of Fungous Infection

Diagnosis	KOH+ H&M+	KOH+ H&M−	KOH− H&M+	KOH− H&M− Culture+	Total of Cases	Total KOH+	Total H&M+	Total Culture+
Dermatophytosis of the hands or feet	20	8	1	0	29	28	21	8
	69%	27.6%	3.4%	0	..	96.6%	72.4%	27.6%
Tinea corporis	19	3	0	0	22	22	19	12
	86.4%	13.6%	0	0	..	100%	86.4%	54.5%
Onychomycosis	79	14	2	0	95	93	81	28
	83.2%	14.7%	2.1%	0	..	97.9%	85.3%	29.5%
Tinea capitis	2	1	0	3	6	3	2	6
Moniliasis (paronychia, intertrigo)	18	1	8	0	27	19	26	25
	66.7%	3.6%	29.7%	0	..	70.4%	96.3%	92.6%
Tinea versicolor	19	0	2	0	21	19	21	0
	90.5%	0	9.5%	0	..	90.5%	100%	0
Total	157	27	13	3	200	184	170	79
	78.5%	13.5%	6.5%	1.5%		92%	85%	44.1%

RESULTS

In 200 out of a total of 340 cases in which examination was made the presence of fungi was demonstrated by at least one of the three diagnostic methods used, namely, examination in potassium hydroxide, Hotchkiss-McManus stain, and culture. Our findings on these 200 cases are presented in the accompanying Table.

COMMENT

The last line of the Table shows that the KOH specimens were positive for fungi in 184 out of 200 cases, or 92%, while the stained preparations showed positive findings in 170 cases, or 85%. It appears that in our hands the traditional method of clearing in a 10% aqueous solution of potassium hydroxide proved in general somewhat superior to the Hotchkiss-McManus stain. The detailed analysis of our findings suggests that the nature of the fungus involved may influence the results obtained with one or the other method of the microscopic examination. In ringworm infections of the glabrous skin and the nails the superiority of the KOH method was evident. In dermatophytosis of the hands or the feet 96.6% of the scrapings were positive for fungi in KOH, as against 72.4% in the stained specimens. In onychomycosis there were 97.9% positive findings in KOH preparations as against 85.3% in the stained specimens. In tinea corporis 100%

2. Pillsbury, D. M., and Kligman, A. M.: A New Histochemical Tool for the Definite Diagnosis of Fungus Infections, Tr. N. Y. Acad. Sc. **13**:145, 1951.

of the KOH preparations showed positive findings as compared with 86.4% of the stained material. The total of all ringworm infections of the glabrous skin and the nails was 146 cases, of which 143, or 97.9%, were positive for fungi in KOH, while 121 cases, or 82.9%, showed positive findings in the stained specimens.

In moniliasis, however, the picture was reversed. Here the stained specimens proved positive for fungi in 96.3% of 27 cases, as against 70.4% of the KOH slides. This fact can possibly be explained by the morphologic peculiarities of Candida albicans in cutaneous material. Its filaments are usually thinner and more transparent and its spores smaller than those of the ringworm fungi. The elements of Candida albicans are also less refractile and are easily overlooked in KOH cleared preparations, while staining shows them very distinctly.

In the diagnosis of tinea versicolor the Hotchkiss-McManus stain also gave better results in our hands than the KOH method, with 100% as against 90.5% positive findings.

On the basis of our findings we would advocate the use of the Hotchkiss-McManus stain in suspected moniliasis and tinea versicolor, but not necessarily for the routine diagnosis of ringworm infections.

We have included in this report some data concerning the cultural studies of our material, although these were not the primary object of this investigation. The percentage of positive cultures in the cases of ringworm infections was not high, namely, 27.6% in dermatophytosis of the hands and the feet, 29.5% in onychomycosis, and 54.5% in tinea corporis. We were surprised to obtain positive cultures in all six cases of nonfluorescing ringworm of the scalp, whereas only three of these were positive for fungi in KOH and two in the stained specimens. The organisms cultured from these six cases were as follows: Trichophyton gypseum (mentagrophytes), two; Trichophyton sulfureum, one; Microsporum lanosum (canis), two; and Microsporum audouini, one.

SUMMARY AND CONCLUSIONS

Two hundred cases of ringworm, moniliasis, and tinea versicolor were diagnosed as mycotic by one or more of the following methods: (*a*) the potassium hydroxide clearing method, (*b*) the Hotchkiss-McManus stain, and (*c*) culture on Sabouraud's medium.

The potassium hydroxide method was found superior to the staining method in ringworm infections, with 97.9% as against 82.9% of positive findings.

The Hotchkiss-McManus staining method was found superior to the potassium hydroxide method in moniliasis, with 96.3% as against 70.4% of positive findings.

In tinea versicolor the Hotchkiss-McManus technique also proved superior to the potassium hydroxide method, with 100% against 90.5% of positive findings.

In six cases of suspected, nonfluorescing ringworm of the scalp the cultures proved superior as a means of diagnosis to either method of microscopic examination.

The Hotchkiss-McManus stain is recommended as superior to the KOH technique for the microscopic diagnosis of moniliasis and tinea versicolor.

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Clinical Notes, New Instruments and Techniques

QUINACRINE (ATABRINE) IN TREATMENT OF LUPUS ERYTHEMATOSUS

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In October, 1951, Francis Page[1] reported in *Lancet*[1] his observations on the treatment of 18 cases of lupus erythematosus with quinacrine (Atabrine) hydrochloride. With the administration of daily doses ranging from 0.1 to 0.3 gm. of the drug 14 patients showed good or excellent improvement of the skin lesions. Three patients showed slight improvement, and in one patient there was no visible change.

These unusually good results in the treatment of a notoriously resistant disease stimulated us to investigate further this form of therapy. We are submitting our observations thus far as a preliminary report.

Thirteen patients, ranging in age from 28 to 80 years, with lupus erythematosus of from 6 weeks to 24 years' duration (Table) were treated with quinacrine hydrochloride. Twelve of these patients had chronic discoid lupus erythematosus, and one (Case 12) had the subacute disseminated form. We prescribed 0.1 gm. of quinacrine hydrochloride twice daily as our usual dosage. After definite pigmentation developed, the dose was in some cases reduced to 0.1 gm. daily. In three cases it was increased to 0.1 gm. three times daily because the eruption did not show early improvement and the patient's skin did not become pigmented on the usual dose.

Nisbet[2] reports a very high incidence of toxic effects in patients receiving quinacrine hydrochloride for prophylaxis and treatment of malaria. Only three of our patients showed evidence of toxic effects. In one (Case 3), a cyclic type of nausea and vomiting which began before the institution of quinacrine therapy on several occasions necessitated either reduction of the dosage to 0.05 gm. two times daily or complete interruption of therapy for a variable period of time. In another patient (Case 8) a mild anemia developed after two and one-half months of treatment, but it responded to iron therapy, permitting resumption of quinacrine administration. A third patient (Case 10) complained of pruritus, which stopped with the interruption of medication and did not recur with its reinstitution.

The duration of treatment varied from three weeks to five months.

The degree of skin staining was variable. It should be noted that the two patients who showed the deepest staining also showed excellent results. On the other hand, there were three patients who showed excellent results with no evidence of pigmentation or only minimal staining. After administering quinacrine hydrochloride in doses of 0.09 gm. one to four times daily to healthy volunteers as well as patients with cutaneous diseases, Miller, Herrmann, and Rubin[3] report that the skin discoloration which occurs as a result of the quinacrine treatment disappears at the end of the third week and does not recur despite continued medication. We

From the Department of Dermatology and Syphilology, Wayne University School of Medicine (Dr. Loren W. Shaffer, Professor).

1. Page, F.: Treatment of Lupus Erythematosus with Mepacrine, Lancet **2**:755, 1951.

2. Nisbet, T. W.: Dermatitis Due to Quinacrine Hydrochloride ("Atabrine"), J. A .M .A. **134**:446, 1947.

3. Miller, O. B.; Herrmann, F., and Rubin, J.: The Effects of Mepacrine Hydrochloride (Atabrine) upon the Human Skin, J. Invest. Dermat. **15**:445, 1950.

did not find this to be true in our short series of cases. In most instances it was possible to detect under Wood's light a fluorescence of the fingernails of the patient taking quinacrine hydrochloride, as has previously been reported by others.[4]

SUMMARY

On the whole, the results shown in this preliminary report (Table) are not as encouraging as those found by the English author. Five patients showed excellent results. Generally speaking, it was felt that those patients in whom the disease process was of the shortest duration showed the best results, although there were some exceptions. Four patients were considered to have shown good improvement, and three demonstrated only slight improvement. There

TABLE—*Results of Quinacrine Hydrochloride Treatment*

Case	Age, Yr.	Sex	Sites of Lesions	Duration	Severity	Dose	Duration of Treatment	Toxicity	Stain	Results
1	80	M	Nose and ears	6 wk.	Moderate	100 mg. b.i.d.	5 wk.	None	0	Excellent
2	39	F	Nose and chin	4 mo.	Moderate	100 mg. b.i.d.	2 mo.	None	++	Excellent
3	41	F	Cheeks, chin, upper lip, and scalp	24 yr.	Severe	50 mg. b.i.d. 100 mg. b.i.d.	6 wk. 2 wk.	Nausea	0	Good improvement
4	42	F	Nose and cheeks	13 yr.	Moderate	100 mg. b.i.d.	5 mo.	None	+	Slight improvement
5	39	F	Face	6 mo.	Moderate	100 mg. b.i.d.	3 mo.	None	0	Good improvement
6	38	F	Face and ears	2 mo.	Moderate	100 mg. b.i.d.	3½ mo.	None	+++	Excellent
7	45	M	Temple and scalp	6 mo.	Moderate	100 mg. q.d. 100 mg. b.i.d. 100 mg. t.i.d.	7 wk. 2 wk. 4 wk.	None	0	No change
8	28	F	Cheeks and buccal mucosa	2½ yr.	Severe	100 mg. b.i.d. 100 mg. t.i.d.	5 mo. 2 wk.	Anemia	+	Slight improvement
9	53	M	Preauricular	1 yr.	Moderate	100 mg. b.i.d. 100 mg. t.i.d.	5 wk. 2 wk.	None	++	Good improvement
10	45	M	Scalp, nose, and cheeks	15 mo.	Slight	100 mg. b.i.d.	4 mo.	Pruritus	+	Good improvement
11	61	M	Cheeks, nose, and ears	2 yr.	Moderate	100 mg. b.i.d.	1 mo.	None	+	Excellent
12	37	M	Subacute disseminated	7 yr.	Moderate	100 mg. b.i.d.	3 wk.	None	+	Slight improvement
13	32	M	Cheeks and nose	8 yr.	Moderate	100 mg. b.i.d.	1 mo.	None	+	Excellent

were no demonstrable changes in the lesions of one patient, even though after a reasonable trial on the usual dosage he received 0.3 gm. of quinacrine (Atabrine) hydrochloride daily for four weeks. The orange-yellow pigmentation of quinacrine hydrochloride also failed to develop, in spite of the larger dose.

As a result of our observations we believe, with Page, that in some cases quinacrine hydrochloride is effective in the treatment of chronic discoid lupus erythematosus. The fact that complete remission was not shown in all cases suggests that it is not, however, specific for the disease. Further investigation will be required to fully evaluate the effectiveness of the drug and to establish the most efficacious schedule for its administration.

Dr. Richard Ferrara supplied the information on Cases 11 through 13, which were under observation at Veterans Hospital, Dearborn, Mich.

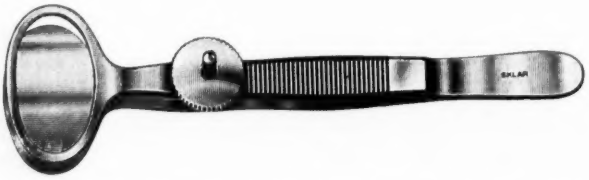
4. Ginsberg, J. E., and Shallenberger, P. L.: Wood's Light Fluorescence Phenomenon in Quinacrine Medication, J. A. M. A. **131**:808, 1946. Kierland, R. R.; Sheard, C.; Mason, H. L., and Lobitz, W. C.: Fluorescence of Nails from Quinacrine Hydrochloride, ibid. **131**:809, 1946.

NEW TECHNIQUE WITH AN OLD INSTRUMENT

ROBERT L. REIN, M.D.
BROOKLYN

The ophthalmologist's chalazion forceps has been adapted for use in dermatologic minor surgery.

The forceps is used to produce reasonable hemostasis in biopsies or in other forms of minor surgery or electrosurgery on small lesions of the sides and tip of the tongue, lips, and external



Desmarres chalazion forceps (product of J. Sklar Manufacturing Co., Long Island City, N. Y.).

ear. The technique is as follows: The lesion is infiltrated with a local anesthetic and then is placed between the "eye" and the solid back of the instrument. The set screw is then turned a reasonable amount to produce hemostasis, and then the indicated surgery is performed.

The instrument is the Desmarres chalazion forceps. Over-all length is 3½ in. (9 cm.); the "eye," or aperture, is approximately 1 in. (2.5 cm.) by ½ in. (1.3 cm.) in diameter.

IMPROVING THE RECOVERY TIME OF HERPES ZOSTER

GEORGE O. BERG, M.D.
LOS ANGELES

Every physician of experience knows that herpes zoster, with its pain and lesions, lasts several weeks. I report four cases of herpes zoster in which antireticular cytotoxic serum Bogomolets was used, with disappearance of the vesicular eruption in two weeks or less.

REPORT OF CASES

CASE 1.—H. F., a man of 60 years, was awakened by severe pain across the right scapula and arm. Two days later, on Nov. 20, 1950, he presented himself for treatment and was given injections of antireticular cytoxic serum and anodynes for local and systemic use, and although photographs showed extension of the area of the lesions nine days later the lesions had regressed so much that he had no pain and did not require further treatment. He received four injections of antireticular cytotoxic serum.

CASE 2.—L. H., a woman of 60, had moderate pain in the flank on Jan. 24, 1952. The next day small vesicles appeared, followed on January 26 by an extensive involvement over the right side and abdomen. Pain was agonizing, and she required the use of narcotics locally in ointments and systemically. She was treated with antireticular cytotoxic serum injections three times a week, and chloramphenicol (Chloromycetin) was used. The lesions crusted and healed in two weeks, although residual pain in the scarred area was present for several months, progressively diminishing after subcutaneous injections of 0.50% procaine hydrochloride (Novocaine) once a week. When last seen the patient was actively engaged in physical work, and the pain was diminishing.

CASE 3.—A. S., a woman of 67, presented herself on March 21, 1952, with lesions of three days' duration over the left buttock. No antibiotics were prescribed, and she was treated with antireticular cytotoxic serum and anodynes locally. The lesions were gone on April 2, leaving no scars, and she was completely free from pain.

CASE 4.—C. B., a woman of 67, presented herself with a well-defined vesicular eruption of herpes zoster extending from the left lumbar region down the side and front of the left thigh. Pain was excruciating. Treatment as outlined above was administered three times a week, and in two weeks the lesions had regressed and the scales had fallen off. Some residual lumbar pain was reduced after one subcutaneous injection of 0.50% procaine hydrochloride, which injections were repeated several times, with lasting relief.

COMMENT

The use of antibiotics, such as chloramphenicol (Chloromycetin) is yet to be evaluated. In my opinion, the patient may possibly receive some psychologic solace through their use. I do not believe that they are therapeutically effective in herpes zoster. Antireticular cytotoxic serum Bogomolets, on the other hand, has appreciably shortened the duration of lesions and pain in the cases cited above.

FAILURE OF DENATURED INSULIN IN THE PREVENTION OF URTICARIA CAUSED BY INSULIN

Report of a Case

LESTER HOLLANDER, M.D.
PITTSBURGH
AND
LYNWOOD D. ZINN, M.D.
CLARKSBURG, W. VA.

In a recent article Dolger [1] stated: "Severe constitutional or generalized allergic manifestations represent a true allergy to the insulin protein itself. This need not be a deterrent to the use of insulin when necessary, since denaturing by heat can yield a physiologically potent insulin without sensitizing properties." He treated four such patients and reported uniform success. Our experience did not corroborate this.

REPORT OF CASE

Mrs. E. G., a 59-year-old childless American homemaker, learned, in 1947, that she had diabetes mellitus. Shortly after she began to use insulin, a very distressing, persistent, and intensely pruriginous flat and lumpy generalized urticaria developed. Since very strict dietary regimen did not control her diabetes mellitus, an extensive trial of the various types and makes of insulin was made. Each one, however, caused a recurrence of the urticaria, and each subsequent episode lasted a longer period.

Two attempts were made to desensitize her to insulin; each one was under the direction of a competent and recognized expert in the management of diabetes mellitus. Both these attempts failed.

The allergic reaction which followed the second attempt at desensitization persisted for a period of four months. It was on account of the latter occurrence that we were consulted on Feb. 11, 1952. In addition to a generalized urticaria, her skin was dry and parched; the latter condition was caused by the lotions, pastes, and antihistamine-containing ointments which she used in a vain attempt to alleviate the intense itching which she suffered.

We stopped all such topical applications and prescribed a diet rich in protein, and we also prescribed large doses of vitamin B complex. She was instructed to apply a hydrous wool fat (lanolin) containing skin emulsion all over her body.

A gradual improvement occurred; the excessive dryness and the generalized urticaria slowly disappeared. The diabetes mellitus, however, remained uncontrolled; fasting blood sugar readings at subsequent weekly intervals were 307, 282, 274, 251, 266, 300, and 270.

1. Dolger, H.: The Management of Insulin Allergy and Insulin Resistance in Diabetes Mellitus, M. Clin. North America **36**:783-790 (May) 1952.

On July 8 she was hospitalized at St. Mary's Hospital at Clarksburg, W. Va., and the desensitization scheme suggested by Dolger [1] was ordered.

A vial of crystalline zinc insulin (Eli Lilly & Company) was denatured by immersion in boiling water for 30 minutes, and 5 units were injected subcutaneously. A mild urticarial reaction appeared within an hour. Subsequent injections of 5 units were given at six-hour intervals. As the general allergic reaction became more and more intense, this trial at desensitization was stopped after a total of 35 units were injected. The patient suffered a severe reaction which lasted six weeks. It subsided slowly under the type of management which had relieved her on the previous occasion.

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USE OF THYMOL AS A PRESERVATIVE FOR FUNGI

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BOSTON

It is often of value to preserve the culture of a fungus for a long period of time. Such preservation not only furnishes the investigator with a permanent mount of the growth, but also allows the instructor to have access to cultures as life-like exhibits for use in demonstrating to his students.

Almost all present-day textbooks [1] suggest that a formaldehyde solution be placed on the cotton stopper of the test tube, in order that the fumes of formaldehyde may kill the growth which has been placed within. The cotton stopper is then pressed slightly down into the tube, and the tube is sealed with paraffin wax.

This commonly used method invariably results in a quick cessation of the fungous growth, but fails as an effective preservative in that, after a few months, the formaldehyde is instrumental in destroying the color of the culture. Inasmuch as the color of the growth is one of the most important characteristics of the fungus and is frequently diagnostic in itself, a method that destroys the color cannot be considered adequate.

Some years ago, I became aware of the deficiency of the formaldehyde method of preserving fungi and instituted a search for more efficient methods. After experimentation with camphor, phenol, and other preservatives, which also proved deficient in this respect, it became evident that a solution of 10% thymol in chloroform would achieve the desired result.

The application of a few drops of such a solution to the stopper of a culture tube has been found to cause prompt cessation of the fungus growth, while subsequent sealing with wax permits safe handling for instructive purposes. Cultures which have been preserved by such a method have retained all their color characteristics for as long as six years, after which time fading has slowly started.

SUMMARY

Ten per cent thymol in chloroform is an efficient and effective fungicide for preserving cultures of fungi.

Thymol does not cause the loss of color characteristics, as does the time-honored preservative, formaldehyde.

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Assistant Professor of Dermatology, Tufts Medical School.

1. Swartz, J. H.: Elements of Medical Mycology, Ed. 2, New York, Grune & Stratton, Inc., 1949, p. 240. Lewis, G. M., and Hopper, M. E.: An Introduction to Medical Mycology, Ed. 2, Chicago, Year Book Publishers, Inc., 1943.

TANGLED HAIR

Bizarre Occurrence After Use of Detergent Shampoo

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WHEELING, W. VA.

The following case of a very peculiar phenomenon, as yet unexplained, is presented.

C. A. S., a 9-year-old white girl, presented herself with a fist-sized matted and tangled wad of hair on the occipital region of the scalp. The mass was felt-like, with groups of long strands protruding from the tangled surface. On July 31, 1951, the mother gave this girl a shampoo using Young Lad Goes West Shampoo, a liquid lauryl sulfate preparation. During the course of the shampoo the hair of the occipital area became unmanageable and in spite of repeated rinsings, a matted and tangled mass proceeded to form spontaneously, which notwithstanding all efforts could not be untangled. The mother said there had been no previous use of wavesets or hair or scalp preparations. Normal-appearing hair of the other areas of the scalp failed to reproduce the phenomenon when again subjected to the shampoo material. Because of the

Tangled hair on occipital area.

failure of prolonged attempts to untangle the hair, it was found necessary to sever it near the scalp. Subsequent hair growth has been normal. Regrown hair in the same area failed to tangle when again subjected to the same shampoo in all dilutions.

Chemical analysis of the shampoo disclosed the following facts: appearance, clear light yellow liquid; solubility in water, complete in all proportions; pH value, 8.4; specific gravity at 25 C., 1.030; total solids (residue at 100 C.), 4.6 gm. per 100 cc.; ash (residue on ignition), 0.37 gm. per 100 cc.; alcohol, glycerin, soap, absent; propylene glycol, 23.7 gm. per 100 cc.; sulfur, calculated as sodium lauryl sulfate, 3.9 gm. per 100 cc.

This case was presented at the May 10, 1952, meeting of the Central States Dermatological Associations, where Dr. George J. Busman and Dr. Francis A. Hegarty presented a patient with an identical case which had occurred within a few minutes after the use of Halo shampoo.

No satisfactory explanation was proposed regarding the tangling and the purely occipital involvement. The possibility of there being a difference in the chemistry of the occipital hair was considered, and the experience of beauticians that synthetic detergents are not generally satisfactory for fine hair was pointed out.

It is hoped that the experience of others with this problem or similar problems will be enlightening.

1300 Market St.

KERATOSIS OBTURANS OTICA

Obstructive Hollow Keratotic Cast of External Auditory Canal

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AND
SEYMOUR FRIED, M.D.
NEW YORK

This is a report of a rare condition observed in a patient in private practice which should be interesting to the otologist as well as to the dermatologist. We can find no previous record of an identical case in the dermatologic texts or literature.

REPORT OF A CASE

The patient, M. O'R., a 38-year-old unmarried Irish-American woman, first noted itching and fullness in her left external auditory canal in July, 1948. At the end of three weeks the

Obstructive hollow keratotic cast of left external auditory canal. Closed at the ear drum end (lower left) and open at the meatus end (upper right).

feeling of obstruction and pruritus in her left ear became unbearable. It was accompanied by headache and loss of hearing on the left side. The discomfort was not relieved until an exact cast in the form of a hollow mold of her external auditory canal was removed. The entire process continued in the left external auditory canal about every three to four weeks. The obstructive mold of keratin had to be removed. The hollow plug was closed at the drum extremity of the external auditory canal and was open at the concha end. It was best removed by irrigation after being loosed with a hydrogen peroxide glycerin mixture.

When examination of the left external auditory canal was performed while the cast was in the process of formation no abnormality could be noted, but immediately following the removal of the cast there could be observed with the otoscope that the surface from which the cast was removed was erythematous and that many pin-point beaded droplets of serous exudation could be observed welling up from the surface to which it had been attached. In the past year the aforementioned symptoms have been forestalled by the removal of the cast by an otologist.

Histologically, the cast is essentially keratin. Fungous scrapings and culture have shown negative results. The process has persisted despite all therapy, including antibiotic ear drops (penicillin, etc.) and radium treatment soon after the removal of the cast.

No relative of the patient has a similar condition. The patient does present some glandular peculiarities of interest. Her basal metabolic rate is + 18, yet she is somewhat obese. She has always had menstrual irregularities and often requires hormone injections to initiate menstruation. If menstruation is delayed, she has severe left-sided migraine headaches, which she has had since she was 14 years of age.

In 1874, Wreden described this condition, calling it "Keratosis Obturans."[1] It was caused by a chronic desquamative dermatitis in which the epithelium was gradually thrown off and accumulated layer by layer in the fundus of the canal. Temporary deafness resulted, the degree of which was according to the extent of occlusion and the proximity of the plug to the drumhead. The cast is often mistaken for cerumen, since its layers may be admixed with and its surface covered by it. A careful microscopic examination will clear the diagnosis. Pain in the external meatus is the commonest symptom in keratosis obturans as described by Wreden. In rare cases, the pain radiates around the ear and over the temporal region.

The condition in our patient differed from that of the case observed by Wreden in that the plug consisted entirely of keratin with no admixture of cerumen and that the plug was hollow and funnel-shaped.

140 East 54th Street, New York 22.

1. Wreden, R.: Arch. Ophth. & Otol. **4**:261-266, 1874-1875.

CONVULSIONS FOLLOWING TREATMENT OF TINEA CAPITIS WITH ASTEROL DIHYDROCHLORIDE OINTMENT

Report of a Case

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BELLEVILLE, ILL.

In the recent literature there has been much written concerning the use of Asterol dihydrochloride (2-dimethylamino-6-[beta-diethylaminoethoxy]-benzothiazole dihydrochloride) in the treatment of fungous infections of all types and in all locations.

Most of the articles stressed the lack of toxicity, both local and systemic, attending the use of this drug. Stritzler[1] reporting on 100 cases of tinea capitis in which Asterol therapy was used made no mention whatsoever of any side-reactions. Ravits,[2] reporting on 100 cases of fungous infection of varied distribution, also emphasized the lack of any toxic effects resulting from the use of Asterol.

In the *Schoch Letter* of March, 1952, Stritzler[3] commented that rarely did hallucinations, convulsions, or ataxia occur after the excessive use of tincture of Asterol on the scalp of young children. As an addendum to the report, the editors quoted Livingood, who stated that it was not necessary for this complication to occur frequently to make it a very disturbing one.

Two examples of convulsions in connection with the use of 5% Asterol in polyethylene glycol (Carbowax) were observed recently.

From the Department of Dermatology, St. Louis University School of Medicine, Dr. Garold V. Stryker, Director.

1. Stritzler, C.; Fishman, I. M., and Laurens, S.: Treatment of Tinea Capitis with New Antifungal Compound, A. M. A. Arch. Dermat. & Syph. **63**:606-610 (May) 1951.

2. Ravits, H. G.: Treatment of Superficial Dermatomycoses with Asterol® Dihydrochloride, J. A. M. A. **148**:1005-1007 (March 22) 1952.

3. Stritzler, C., in "Schoch Letters," Penicillin Research Center, Southwestern Medical Foundation, Dallas, Texas, March, 1952.

REPORT OF CASE

T. B., a 3-year-old white boy, entered the hospital for the treatment of convulsions. The history obtained from the mother was that four weeks previous to the onset of the convulsions the child had fallen down the stairs. No serious effects were noticed. Four weeks later the convulsions began. On further questioning it was learned that for the eight weeks previous and up until the onset of convulsions the child had been treated for tinea capitis. The therapy consisted of rubbing Asterol ointment into the child's scalp twice daily.

While the child was in the hospital, the house staff noticed marked personality changes occurring in him. He became mean, irritable, negativistic, and he had numerous temper tantrums.

Skull plates, ventriculograms, neurological examinations, and spinal fluid examinations all showed normal results. There was no evidence of hydrocephalus or papilledema. Electroencephalography revealed a picture consistent with convulsive disorder but without any definite localization.

The temperature rose to 101 F. daily in the afternoon. It was normal in the forenoon. The convulsions gradually decreased in severity and number until the child was discharged.

Laboratory tests showed a progressive leucopenia until a low of 2,700 white blood corpuscles per cubic millimeter was recorded. The lymphocytes gradually increased until they reached a high of 80%. This blood picture gradually returned to normal as the condition of the child improved.

The history and time relationship of the second case, observed at another hospital, bears a striking resemblance to the case reported.

COMMENT

This report was not written with the intention of discrediting a worth-while preparation, but merely to point out a frightening and unusual relationship between the prolonged use of Asterol ointment on the scalp of children and the development of grand mal seizures. If this relationship is more than coincidental it deserves to be brought to the attention of the medical profession, since Asterol is being widely used in the treatment of tinea capitis.

In conversation and correspondence with other dermatologists, I find that the above sequence of events is being observed in other sections of the country.

Correspondence

CONVULSIONS FOLLOWING TREATMENT OF TINEA CAPITIS WITH ASTEROL DIHYDROCHLORIDE OINTMENT

To the Editor:—Sporadic reports about temporary disturbances of behavior and about neuromuscular disorders in infants and children under treatment with Asterol dihydrochloride (2-dimethylamino-6-[beta-diethylaminoethoxy]-benzothiazole dihydrochloride) prompted us to caution the medical profession by all appropriate means against the use of Asterol ointment and Asterol tincture in infants. Thus, pertinent warning statements have been included on the labels of these products and in our house literature for an entire year.

Unfortunately, these warnings went unnoticed only too often. On the other hand, many physicians were undoubtedly influenced to desist from the use of Asterol for children generally, even for those over 2 years of age.

In the earnest effort to clarify the meaning and intent of our warning statements and to dispel any misgivings on the part of dermatologists to prescribe the drug for children over 2 years, the following objective report on the central nervous system effects of Asterol was prepared.

When Asterol was submitted to the Federal Food and Drug Administration, there were filed reports from some 40 groups of investigators covering close to 2,500 patients. Among these patients there were 746 cases of tinea capitis, and it seems reasonable to assume that many more children had been treated with Asterol by that time. Subsequently, Asterol was used for approximately three months for over 800 children afflicted with tinea capitis in Sault Ste. Marie, Ont., Canada. In none of all these instances were any effects on the nervous system reported, although some of the patients received the medication twice daily for periods of up to six months. Similarly, no report of neurotoxicity of the drug was made to us in connection with a chronic toxicity study in 40 adults.

It was only during the period of general availability of Asterol that reports about neurotoxic symptoms attributed to the drug came to our attention. To date, a total of 39 such cases, 16 of which involved infants, have been encountered.

The total figure includes 16 cases in which either quite unusual situations were represented (3 cases), or in which there obviously existed no causal relationship between the Asterol medication and the neurotoxic manifestations observed (6 cases), or on which there is almost no information available other than that neurotoxicity was encountered (7 cases).

As an example of the first group, there is the case of a woman who experienced a "wave of emotion upward over her body" after having sprayed her vulva with Asterol tincture every 30 minutes for several days (we explicitly warn against the use of Asterol on mucous membranes in our caution statements).

As cases illustrative of the second group, the following instances are mentioned: an infant in whom neurotoxic symptoms appeared one month after discontinuation of Asterol therapy; a child whose emotional disturbances "antedated the use of Asterol"; and two children who were reported to have had hallucinations during the first course of therapy, but failed to display the phenomena during the second course.

Finally, as instances representative of the last group, the following cases are cited: a child in whom the report of toxic phenomena represented little more than hearsay and two cases in which Asterol therapy was incriminated without any substantiation of the facts.

This then leaves 23 patients for further discussion, whose age distribution was as follows: 2 weeks to 2 years, eleven (the age of ten of these infants ranged from 2 weeks to 6 months and one was 19 months old); 2 to 3 years, two; 3 to 4 years, five; 4 to 5 years, three, and 5 to 7 years, two.

It is obvious that the incidence of reactions reported must have been much higher among infants, since without doubt many more children than infants must have been treated with Asterol.

The infants were treated for thrush, tinea cruris, tinea corporis, and poorly defined skin conditions. For two infants 2% Asterol citrate solution (experimental) and for one 5% Asterol tincture, diluted 1 : 5, were applied to the oral mucosa. One was treated with 2.5% Asterol ointment in a vanishing cream base (experimental) and seven with 5% Asterol ointment.

All children over 2 years were treated for tinea capitis with the exception of one who had generalized moniliasis. In four instances 5% Asterol tincture was used, in six, 5% Asterol ointment, and in two, both preparations.

For the majority of these 23 patients, the amounts of Asterol employed do not seem to have been excessive.

The period of treatment before appearance of symptoms ranged from three days to four months in the infants and from one to eight weeks in the children.

As for symptomatology, all the infants went into convulsions, but of the 12 children with neurotoxic symptoms only 5 experienced episodes of seizures. In addition, one of the latter had hallucinations, a symptom which was also exhibited by six of the other children. In several of the patients there were a variety of other neurotoxic and systemic reactions, either singly or combined, such as ataxia, listlessness, tremors and twitching, exaggerated reflexes, and rolling of the eyes. Cyanosis and loss of appetite were recorded for two infants each, and behavior changes were recorded for one infant and four children. One of the latter exhibited mental deterioration, a symptom reported for another child also.

It is worthy of note that all five children who experienced convulsions were 3 years old or younger. In contrast, convulsions were not reported to have occurred in the six children who were 3½ years of age or older, and in one child who was 2½ years old. Five of the six had hallucinations, and one had milder neurotoxic symptoms.

Information on the time relationship between discontinuance of Asterol administration and return to normal was obtained on 7 of the 11 infants and on 9 of the 12 children. In four of the infants neurotoxic symptoms disappeared in a matter of a few days, in one the return to normal took two weeks, in one three weeks, and in one almost two months. In two of the children neurotoxic symptoms disappeared in a matter of a few days, in three in from one week to 10 days, and in two each in three weeks and one month respectively.

In appraising the neurotoxic potentialities of Asterol, we must project the number of cases of central nervous system disturbances reported against the over-all distribution picture. If we define arbitrarily both a 1 oz. (30 gm.) tube of Asterol ointment and a 2 oz. (60 cc.) bottle of Asterol tincture as a "unit" and if we furthermore convert the sample tubes and the 1 lb. (454 gm.) jars of ointment and the sample bottles and the 16 oz. (480 cc.) bottles of tincture into 1 oz. (30 gm.) tubes and 2 oz. (60 cc.) bottles, a total of 1,558,915 "units" of Asterol were distributed up until January 1 of this year. (This figure does not include the Asterol dusting powder distributed.)

Furthermore, if we arbitrarily assume that a patient would use an average of five "units" of Asterol—and this certainly is more than liberal—a total of 311,783 patients must have used the drug. Taking into consideration all 39 cases of neurotoxicity reported, i. e., *not* excluding those instances which represented quite unusual situations, in which a causal relationship between Asterol medication and neurotoxic symptoms can be ruled out and on which entirely inadequate information is available, the incidence of central nervous system reactions occurring after the use of Asterol would be 0.0125%. By the same token, one out of 7,994 patients might have experienced this type of side-reaction.

Carrying these calculations a step further, if we assume that the warning against the use of Asterol in infants will be observed in the future, it may be anticipated that in no more than 23 patients (i. e., excluding 16 who are infants from 39 patients) out of approximately 311,000 using Asterol central nervous system disturbances may develop. This is an incidence of approximately 0.007% or one out of 13,521 patients. Obviously, this incidence of central nervous system disturbances may be expected to occur also in persons not treated with Asterol.

There is no way of calculating the incidence of neurotoxic reactions applying to children specifically, since one cannot judge the portion of the total distribution of Asterol "units" which were used in pediatric practice. However, Wilson and others (*J. A. M. A.* **150**:1002, Nov. 8, 1952) estimated the incidence of neurotoxicity to be "less than one per thousand children of all ages who are receiving treatment" with Asterol.

It will be noted that in the above calculations the most stringent yardstick was employed. In this connection, attention is invited to the fact that all neurotoxic reactions reported to the day of this writing were included, but the distribution figures only to January 1.

No doubt, the suspicion that Asterol may occasionally cause central nervous system disturbances in a child is justified. However, Asterol was actually proved to have been the offender in only one patient, namely, the 4-year-old boy reported by Wilson (mentioned above), who after recovery from hallucinations and tremors experienced while under treatment with 5% Asterol tincture was reexposed to the drug and in whom neurotoxic symptoms again developed.

In summary, if the use of Asterol is barred in infants and if the total dose administered to children ranging in age from 2 to 10 years is limited to 2 oz. (60 gm.) per week, as will be done in recently adopted revised warning statements, the danger of producing neurotoxic symptoms is remote indeed. However, the medical profession is urged not to use Asterol for infants (up to 2 years), to limit the total quantity of Asterol ointment and/or Asterol tincture to 2 oz. per week, to follow closely the case of children undergoing treatment with the drug, and to discontinue its use if any signs suggestive of neurotoxicity occur.

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LICHEN SIMPLEX CHRONICUS IN ORIENTALS

To the Editor:—In their article, "Lichen Simplex Chronicus in Orientals" (A. M. A. ARCH. DERMAT. & SYPH. **66**:612-617 [Nov.] 1952), Dr. Charles R. Rein and Dr. B. Leonard Snider very aptly stress the higher incidence of this dermatosis in oriental patients. This higher incidence is of considerable interest, because its explanation might throw some light on the question of the pathogenesis of circumscribed neurodermatitis.

Having practiced dermatology for more than nine years in Shanghai, I should like to add a few remarks to this very interesting and important question, based on my knowledge of the local conditions there. When I started my dermatological practice in China, in the National Medical College of Shanghai (head, Dr. F. Reiss), one of my first impressions was the relatively high incidence of this dermatosis, localized on the neck, in the native population. In the statistics of Yang, from the same hospital, quoted by Rein and Snider, the incidence of lichen simplex chronicus is 4%. A very similar incidence of the dermatosis is observed in the white population of the United States. This statistical comparison is, in my opinion, misleading. In order to make any comparison, we have to take into consideration the very high incidence of scabies, of mycotic and pyogenic dermatoses, and of syphilis, especially in the above-mentioned hospital, frequented by the Chinese poor, before comparing it with the incidence of the same disease in the Chinese residing in the United States, where the incidence of the above infestation and infections is considerably lower. A very conservative estimate of the incidence of the diseases mentioned above, taken as a group, in the clinics of the National Medical College of Shanghai would be 60%. In consequence, in order to compare the incidence of lichen simplex chronicus in the Chinese in their homeland with the incidence of the same dermatosis in the Chinese residing in the U. S. A., where the incidence of the above infestation and infections is relatively low, the figure of 4% should be at least doubled. I would be hesitant to accept as a fact the higher incidence of lichen simplex chronicus in the Chinese living in the U. S. A. as compared with the incidence in the Chinese living in China.

Regarding the occurrence of lichen simplex chronicus in the Chinese, I would stress, on the basis of my experience, the preponderant localization of the dermatosis on the sides of the neck, when compared with the localization on the nape of the neck. I am inclined to think that the higher frequency of the dermatosis in the Chinese is due in the first place to the clothing, which coming in close contact with the neck, causes contact dermatitis which is modified in its appearance and which soon takes on the characters of lichen simplex chronicus. A similar sequence of events was described by G. A. Grant Peterkin in his article, "Textile Dermatitis in Men" (ARCH. DERMAT. & SYPH. **58**:249-264 [Sept.] 1948) as regards contact dermatitis from the khaki drill shirt: "If the shirt was worn for several months, the papular rash became a weeping, crusted dermatitis and finally became indistinguishable from a plaque of circumscribed neurodermatitis associated with intense pruritus." I think that it would be timely to make patch-test studies with the materials of clothing, applied to the skin after being soaked in the sweat of the patients, in a similar way as recommended by Peterkin in the above mentioned article.

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Society Transactions

BRONX DERMATOLOGICAL SOCIETY

William Leifer, M.D., *President*

Henry Silver, M.D., *Secretary*

April 17, 1952

Beryllium Granuloma and Ulceration of Fingers: Rapid Improvment with Cortisone Ointment. Presented by DR. ALEXANDER A. FISHER.

Mr. J. P., aged 28, was previously presented before the Society on Jan. 17, 1952. He had cut his fingers on a fluorescent bulb on Sept. 5, 1951, following which occurrence ulcerative and granulomatous lesions developed.

The consensus was that the lesion should be excised and a plastic repair done.

Dr. E. M. Kline, medical consultant of the General Electric Company, also stated that there was no contraindication to excision of the granulomatous skin, in spite of the fact that there was some osteoporosis in the underlying bone.

However, since there have been reports of successful use of cortisone in constitutional berylliosis, it was decided to try cortisone in ointment form in this case.

On March 31, 1952, treatment with an ointment containing 5% cortisone was instituted, followed by rapid improvement.

DISCUSSION

DR. ALEXANDER A. FISHER: We decided to try 5% cortisone ointment, and there seemed to be improvement. The ulcer now appears to be cured.

DR. MARION B. SULZBERGER: Can Dr. Fisher tell us anything about the effect of cortisone in the treatment of beryllium poisoning in general, when given systemically?

DR. HENRY SILVER: When the case was first shown, I was among those who suggested radical surgery. Until now, only failures have been recorded with all forms of topical treatment. Dr. Fisher's report of a successful treatment is therefore very encouraging.

DR. ALEXANDER A. FISHER: There have been two cases reported of generalized berylliosis cured by cortisone. In cases with constitutional effect I do not know what cortisone does to beryllium. But until now there has been treatment by surgery in all the localized cases. The physician of the Consolidated Edison Company advised me that this condition will probably cease to appear, because since 1949 beryllium has not been used in fluorescent bulbs. There are, however, a few old ones in circulation, and an occasional case may still be encountered.

Hereditary Leptocytosis (Cooley's Anemia) with Ulcers of the Leg and Renal Calculi. Presented by DR. ALEXANDER A. FISHER and (by invitation) DR. SAMUEL SCHWARTZ.

I. D., a woman aged 31, comes from a family in which there are several cases of hereditary leptocytosis (Cooley's anemia).

Nine years ago she received sclerosing injections, following which ulcers developed on the legs. The ulcers have been resistant to all types of treatment.

Recently, there has been some improvement following grenz ray treatments. Of the many ointments which have been applied, Rayderm ointment (an antihistaminic which contains euphorbia, phenyl salicylate, neatsfoot oil, cod liver oil, olive oil, hydrous wool fat U.S.P. [lanolin], oxycholesterol, and cetyl alcohol) has been the most comforting to the patient.

The patient has had renal calculi recently.

The family history (detailed in *Am. J. Science* **13**:46 [July] 1952) is as follows: The father died of splenomegaly at the age of 38, and the mother, aged 63, is a diabetic. Ida, the patient, aged 31, has Cooley's anemia and ulcer of the leg. Her brother, Nick, has hypochromic anemia; her sister, Ann, has anemia of a second degree with occasional nucleated red blood cells; Joan and Carol, Ann's children, aged 4 and 9 respectively, both have Cooley's anemia; Frank, another brother of the patient, died at the age of 12 after a "stomach operation"; another brother, Arthur, aged 34, had Cooley's anemia, and Mike, another brother, died at the age of 40, with Cooley's anemia. Mike's children, Mike and Frank, 4 and 6 years old respectively, are normal.

DISCUSSION

DR. DAVID BLOOM: The history as given does not contain findings that make definite the diagnosis of Cooley's anemia. This disease is of interest to me because it is a hereditary condition, and, as in sickle cell anemia, the heterozygotes show minor manifestations whereas the homozygotes are severely affected. I learn for the first time about leg ulcers occurring in connection with Cooley's anemia.

DR. SAMUEL SCHWARTZ (by invitation): The woman, aged 31, like the other affected members of her family, has been known to me for about 14 years. These patients at one time or other were all hospitalized for complications and work-ups, and the diagnosis of Cooley's anemia has been confirmed.

This disease is a familial entity peculiar to inhabitants of the north shores of the Mediterranean. The first clue that led to the separation of this anemia from others was the distinct resemblance to the Mongolian race that patients with the condition acquire during the course of the disease. This appearance is due to a yellowish pigmentation of the skin and to the progressive thickening of the malar eminences and the skull. Other characteristics of the disease are a severe refractory anemia, a low hemoglobin content, an abundance of nucleated red blood cells in the peripheral stream, and bone changes in the form of thinning of the cortex, due to proliferating marrow, extreme splenomegaly, and less degree of hepatomegaly. Initially, all cases were considered to be severe, progressive, and fatal. Recently, evidence indicates that the disease shows a range of severity from extremely mild to grave forms. This view is based on the fact that studies of siblings and parents of patients with advanced forms have revealed a high incidence of persons who show milder activity of the disease.

Incontinentia Pigmenti(?) with Atrophy of the Skin of the Thighs. Presented by DR. ALEXANDER A. FISHER and (by invitation) DR. D. DEXTER.

L. T., a girl infant aged 11 months, had blisters and crusting at birth and was placed in the isolation ward of the hospital. The blisters and crusting persisted until she was 2 months of age, at which time the present lesions appeared.

The eruption is more or less generalized except for the face; it is light brown and most pronounced on the lateral aspects of the chest and abdomen. It consists of linear bizarre streaks, spidery forms, and discrete macules. For the past year there has been no change in the eruption. The general health of the child is good, except that it is somewhat underweight.

Examination of the blood showed 62% (8.9 gm.) hemoglobin content, 3,720,000 red blood cells, 0.68 color index, 8,350 white blood cells, with 29% neutrophiles, 66% lymphocytes, 4% monocytes, and 1% eosinophiles. The erythrocytes exhibit a marked increase in central pallor.

DISCUSSION

DR. MARTIN B. SULZBERGER: This is a beautiful case. First, the bizarre arborization in distribution of the pigment is so typical that there is no doubt about the diagnosis at first glance. Secondly, with reference to this history of blisters and crusts, this is not at all unusual in these cases. Quite possibly, the incontinence of pigment is secondary to some form of cutaneous damage, either intrauterine or after birth. Many patients with incontinentia pigmenti have various associated defects in other organs, like the eyes, brain, teeth, etc. As far as I know, the pigmentary changes have been permanent in all cases which have been followed through the years.

Fixed Drug Eruption Due to Sulfadiazine. Presented by Dr. David Ballin.

C. P., a white man aged 19, was first seen on March 13, 1952, presenting a number of dark brown, macular areas on the right eyebrow, the trunk, and the extremities.

The past history was not contributory, except for the history of the intake of sulfadiazine.

Routine serologic tests for syphilis gave negative reactions.

Histologic examination by Dr. C. F. Sims showed a slightly irregular epidermis. There was an increase of pigment in the basal cells as well as in chromatophores in the upper corium. Some of the pigment macules were extracellular. A mild perivascular banal infiltration was present about the vessels of the upper cutis. The histologic diagnosis was fixed drug eruption. At this showing the patient has a positive reaction to ingestion of 0.5 gm. of sulfadiazine in the form of itching and erythematous haloes around all the lesions.

DISCUSSION

Dr. Marion B. Sulzberger: This is a classic case. I should like to know whether I am right in believing that these cases are rare now. Why is that? In the old days, for example, when Dr. Abramowitz and Dr. Wise were in practice, such cases were common, not only due to the use of phenolphthalein, but to many other drugs. What has happened that these cases have almost disappeared?

Dr. Alexander A. Fisher: One possibility is that dermatologists do not bring these cases to meeting as frequently as formerly.

Dr. John Garb: It is possible that a tolerance to this drug may develop in a person by the repeated ingestion of sulfadiazine, similar to the case reported by Dostrovski and Sagher (Fixed Erythema Due to Sulfanilamide with Gradually Lessening Sensivity, Arch. Dermat. & Syph. **49**:418 [June] 1944). In that case the intensity of the reaction to sulfanilamide was gradually reduced during the course of 10 months, when the patient was given the drug at irregular intervals.

Dr. Marion B. Sulzberger: It would be interesting to discover, by testing this patient with different sulfonamides, just how much cross reaction exists between the various sulfonamides, and then by going on to other derivatives, to see how wide the sensitization is. If we could get this patient to cooperate sufficiently, and if we could study him for many years, the findings might have great immunological significance. I think one of the reasons why these eruptions are seen so rarely now is simply that the patients themselves, and the nondermatologic public at large, have come to recognize them and do not come to the doctor to be treated. With reference to the discussion of Dr. Garb, habituation and spontaneous increase in tolerance on continued exposure to the drug are very common in drug eruptions and are not necessarily due to specific desensitization.

Dr. Rudolf L. Baer: The problem of spontaneous desensitization requires much further study. There is some evidence that it not only occurs in drug sensitization but also in allergic eczematous sensitization and perhaps also in tuberculin-type sensitization. The recent literature, for instance, reports the disappearance of sensitivity in proved cases of chancroid, as for example, in a study at Goldwater Memorial Hospital (*J. Allergy* **21**:344 [July] 1950) in which Dr. White and I showed that 20% of patients deliberately sensitized to 2-4 dinitrochlorobenzene as shown by the occurrence of a spontaneous flare-up no longer were hypersensitive several weeks later, while in the remaining 80% a more persistent sensitivity had developed. We were unable to follow that group of patients to ascertain whether the sensitivity to 2-4 dinitrochlorobenzene recurred or whether the desensitization was permanent.

Dr. Marion B. Sulzberger: Many forms of specific hypersensitivity of the skin tend to disappear after persisting for variable lengths of time, and other forms rarely, if ever, disappear spontaneously. For example, the positive Frei reaction rarely disappears spontaneously. In general, the acquired changes due to infection rarely are lost. But some food sensitivities, drug sensitivities, poison ivy sensitivities, etc., disappear after many years. Old people in general tend to lose many sensitivities, so that the skin of old people is much less reactive when it is tested

with a variety of allergens than is the skin of younger people. It is, of course, interesting to speculate on the possible role of hormones (e. g., steroids) in those cases of cutaneous sensitivity with age. Many of the antibiotics like penicillin, sulfonamides, and other drugs as well, cause an eruption at one time, and then, on continued administration, may cease to cause trouble. This occurs spontaneously in numerous cases but in all those cases in which this does not occur "spontaneously" whenever we tried to produce desensitization deliberately or to increase the tolerated dose of drugs, we failed.

DR. DAVID BALLIN: This patient has had the sensitive status for about 5 months. He received 0.5 gm. of sulfadiazine, with distinct reaction occurring. With regard to Dr. Sulzberger's remarks, I still see patients in whom fixed eruptions occur from continued use of the arsphenamines.

Xanthoma Tuberosum in Three Generations. Presented by DR. DAVID BLOOM.

Case for Diagnosis (Keratoderma Blennorrhagicum? Psoriasis?). Presented by DR. ABRAHAM J. ORFUSS.

Acrodermatitis Chronica Atrophicans? Poikiloderma Vasculare Atrophicans (Jacobi)? Presented by DR. ALEXANDER A. FISHER.

Case for Diagnosis (Folliculitis Decalvans?). Presented by DR. ANDREW FRANKS.

Case for Diagnosis (Dermatitis Herpetiformis? Bromide Eruption?). Presented by DR. ALEXANDER A. FISHER.

Case for Diagnosis (Lichen Planus? Dermatitis Medicamentosa?). Presented by DR. NATHAN SOBEL.

Fibromatous Nevus. Presented by DR. IRWIN I. LUBOWE.

Amyloidosis Cutis. Presented by DR. JOHN GARB.

Morphea with Pronounced Infiltration. Presented by DR. ABRAHAM J. ORFUSS.

CHICAGO DERMATOLOGICAL SOCIETY

James R. Webster, M.D., President

Irene Neuhauser, M.D., Secretary

May 21, 1952

Porokeratosis (Mibelli). Presented by DR. H. H. RODIN, South Bend, Ind.

The patient, C. G., a white man aged 69, in good health except for the lesion involving the right hand and forearm, was first seen on Feb. 28, 1951. He complained of a deforming lesion involving the hand and forearm of 18 to 20 years' duration. He stated that the lesion began as a small wart-like growth on the back surface of the hand and has gradually spread to involve most of the forearm. The deformity has now reached the stage where the hand has lost all function. The ulcers involving the dorsal surface of the hand and wrist developed approximately seven years ago, two or three years after he had received the last x-ray treatment.

He has received a great deal of treatment in the form of topical medication, cautery, antibiotic administration and x-ray therapy, without benefit.

Dermatological examination revealed a sclerosing and atrophic dermatosis involving the right hand and forearm. Two large ulcers with granulomatous bases and elevated sclerotic borders are present over the dorsal surface of the right hand and wrist. The margin of the principal lesion has an arciform border which extends from the center of the palm to the upper third area of the forearm. This border has a keratotic ridge containing a central gutter from which arises a corneous lamella.

Peripheral blood and urine are normal. The serological test gave a negative reaction.

The surgical and medical history is uneventful and bears no relation to his present condition.

A biopsy specimen removed from the border was submitted to the Armed Forces Institute of Pathology, Washington, D. C., and their report in part is as follows:

"Several members of the staff who have studied this specimen have agreed to the diagnosis of Porokeratosis (Mibelli)."

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: It is difficult to accept this as an example of porokeratosis. The clinical features of this very rare disease conform in every case to a distinct pattern, in which a crater-like depression exists in an elevated border. The existence of

ulceration here is more suggestive of a neoplasm. A biopsy of the lower portion of the lesion should establish the diagnosis. I hope that this may be reported at the next meeting.

DR. S. W. BECKER: I saw this man about four years ago at the Mayo Clinic, after he had been there for some time. When he first came to the Clinic the clinical picture was definitely that of blastomycosis. However, the microscopic examination and the smears revealed no organisms, and, finally, because of this hyperkeratotic rim in the process with the microscopic study, a definite diagnosis of porokeratosis Mibelli was made.

The ulcer which Dr. Wile mentioned as possibly being caused by malignant degeneration may be the result of a nutritional deficiency. He has now on the back of his hand one vegetative plaque which still resembles blastomycosis, and he also has this other ulcerative lesion with the border which suggests a squamous cell carcinoma. I think that a biopsy should be made of this to see if there is carcinoma.

DR. FREDERICK R. SCHMIDT: I should like to point out that lesions of porokeratosis Mibelli may occur in the mouth. I have a photograph of such a lesion on the inside of the cheek, showing an atrophic center surrounded by a raised keratotic wall. Histologic examination showed the "cornoid lamella" composed of a column of parakeratotic cells.

DR. H. H. RODIN, South Bend, Ind.: In considering the differential diagnosis in this case it must be kept in mind that the lesion started as a verrucous papule approximately 18 to 20 years ago and has slowly progressed as a sclerosing lesion to involve the hand and most of the forearm. It is also important to note that the margins have always presented a sulcus or gutter containing the corneous lamella.

The ulcerative lesions which resemble blastomycosis have only been present for the past seven years. Biopsies and cultures of these lesions have been made on several occasions in the hope that the Blastomycetes could be found, but these tests always gave negative results. Since he has received an unknown amount of roentgen therapy to this area, these lesions probably represent ulcerative sequelae.

These lesions were examined under Wood's light, and a fluorescence resembling "glowing" coal was observed at 5:00 and 6:00 o'clock in the border of one of the ulcers. It is my understanding that Dr. Ronchese has reported this finding as indicative of malignant degeneration. A biopsy will be performed in this area as soon as possible.

(Note: Histological examination revealed a squamous cell carcinoma, Grade II, in the tissue removed from this area.

This patient was seen at the Mayo Clinic several years ago, and, as Dr. Sam Becker has stated, a diagnosis of porokeratosis was also made.)

Acrodermatitis Chronica Atrophicans. Presented by DR. A. W. STILLIANS.

Mr. O. L., a 51-year-old civil engineer born in Alsace-Lorraine, suffered an injury to his lumbar spine (a slipped disc he was told) in June, 1948. A few months later he noticed redness of the skin of his right knee and then similar redness of the right foot. This slowly gave place to wrinkling of the skin. The process spread about the knee and upward on the thigh. During wet weather he has pain in the right ankle, knee, and hip.

The skin about the knee and along the outer side of the thigh is thin, loose, and wrinkled, and the venules show distinctly through it.

Little atrophy is seen in the lower part of the leg or in the foot. No such changes are seen elsewhere.

The hemoglobin content is 90%; the white blood cell count is 12,400, with 25% lymphocytes, 64% polymorphoneutrophiles, 3% monocytes, and 3% eosinophiles. The sedimentation rate is 6 mm. per hr. The Kahn test was negative. Urinalysis revealed no albumin or sugar.

DISCUSSION

DR. S. W. BECKER: It is a pretty well-known fact that this disorder is seen chiefly in foreign-born persons. To date, I have never seen anyone born in this country who has this disorder. In Paris, this disorder is rarely seen, but as near by as Strasbourg, where the racial

characteristics of the people are beginning to be different, there are a great many more of these patients. Professor Pautrier said he almost never saw it in Paris, but when he went to Strasbourg there were many of these patients, and he has written many excellent papers on the disorder.

DR. FREDERICK R. SCHMIDT: I have always suspected that Pautrier's patients with this disease originating in the Vosges mountains of Alsace-Lorraine and Oppenheim's patients from Czechoslovakia and Poland had this disease because they had frozen their feet when they were young. If you have seen these people living in these localities, you know that they live in damp homes. This fact may also account for the high percentage of tuberculosis of the skin in these areas. The vascular damage caused by exposure to cold leads to collagenous disease, in my opinion. Montgomery believes that this collagenous disease is the primary cause in this process (Montgomery, H., and Sullivan, R. R.: Acrodermatitis Atrophicans Chronica, ARCH. DERMAT. & SYPH. **51**:32-47 [Jan.] 1945). In South America, especially in Chile, many people freeze their feet because they wear no shoes, and there I saw a good many examples of this disease.

DR. UDO J. WILE, Ann Arbor, Mich.: I believe I am correct in stating that the majority of patients with this disease are middle-aged or elderly women, particularly those of an asthenic type. Under the circumstances, these facts do not seem to fit in with the history of frozen feet in early life.

Ulcerative Stomatitis? Presented (by invitation) by DR. GEORGE C. WELLS.

The occupation of Mr. H. C. H., aged 38, is that of butcher.

This man has had soreness in the mouth since January, 1952. When this trouble started he was being treated for hyperthyroidism with potassium iodide.

During the last three months he has been treated with penicillin and chloramphenicol (Chloromycetin) systemically, and with methylrosaniline chloride (gentian violet), aureomycin and terramycin mouth washes, and with local anesthetic preparations for the soreness in the mouth. There has been a steady progression of the mouth ulceration, and he feels that nothing has done him any good.

There is extensive superficial ulceration on the tongue, lips, buccal mucosa, and palate, and the process extends down to the glottis. There is much ragged epithelium, and some of the areas are purulent. There is moderate lymphadenopathy of the neck.

Cultures from the mouth have grown hemolytic streptococci and hemolytic staphylococci. No Candida was seen in potassium hydroxide preparations. Smears from the buccal mucosa showed numerous epithelial cells and pus cells, but no Tczanck cells.

Chest x-rays show apical shadows, probably old scarring.

The blood cell count was normal. The Kahn test was negative.

DISCUSSION

DR. ADOLPH ROSTENBERG JR.: Many possibilities have been thought of from a bacteriological standpoint. I should merely like to suggest the possibility of a viral origin, even though the case does not particularly resemble a viral infection.

Another possible cause would be that this man is sensitive to the food or to an amalgam or that some other dental source provides continuous irritation. These are only speculations for which there is no evidence.

DR. PAUL WEICHSELBAUM: This patient was followed for approximately one month at the University of Illinois Dispensary. We could find nothing of significance mycologically or bacteriologically.

He was referred to Dr. Maury Massler of our Dental Therapeutics Department. Dr. Massler has collected six cases of this particular malady to date, and he says that they all follow a definite pattern. They all have a sudden onset, are exceedingly chronic, and subside without treatment. Dr. Massler has done virus studies, but can offer no help as to the etiology.

This patient had some amelioration of symptoms for several weeks after the use of aureomycin mouth wash. Then he experienced a recurrence of the ulcers, with severe pain. Dr. Massler has titled this disease desquamative gingivitis.

Dr. H. H. Rodin, South Bend, Ind.: In addition to the usual precipitating factors of the viral ulcerative stomatitis such as food allergy, drugs, and infection, one should also consider the possibility of an ulcerative colitis. Recently we had the opportunity to observe such a case in which the aphthous stomatitis was the only objective symptom.

Dr. George C. Wells (by invitation): I am very grateful to the discussers for their helpful suggestions. I might say that the consensus at the University of Chicago was in favor of pemphigus because of the rather ragged epithelium and because the man himself said he had seen bullae in the mouth. However, I am not altogether in agreement. I certainly could find no pemphigus cells in the smear, but I still find smears from the mouth difficult to interpret in regard to pemphigus.

This man is extremely neurotic and very difficult to help. He takes a great interest in his disease, and I wondered if he were using anything to produce fresh lesions. However, the lesions extend down as far as the arytenoids, and this makes artefact unlikely.

Blastomycosis Dermatitidis. Presented (by invitation) by Dr. Jack Rodriquez.

A. F., a 62-year-old well-developed white man, states that he was entirely well until 1932 when hydrocele developed on the left side of the testicle. This was aspirated once or twice yearly. In 1941 a "boil" developed in the same area which eventuated in a fistula. In 1942 the patient underwent surgical removal of the left testicle. One month following surgery, an oozing sore developed in the left inguinal region, for which the patient consulted Dr. Ormsby who diagnosed it as blastomycosis and gave the patient iodides. The original lesion healed, but by peripheral extension involvement of the crotch and perineum of the same side occurred. Because of the slow progress, the patient went to the Mayo Clinic for consultation and was again told he had blastomycosis and given iodides.

During 1950 to 1951 the patient has had six x-ray treatments for the area, without benefit. He is currently taking approximately 200 grains (12 gm.) of potassium iodide daily.

There is a sharply circumscribed lesion involving the left inguinal, crotch, and perineal area. The upper part of this lesion is healed, with depigmentation and superficial atrophy. The lower part is grayish-brown and moderately verrucous and granulomatous. This lesion encroaches closely upon the anus.

The white blood cell count was 11,500; the hemoglobin content was 14.9; the Kahn test was negative; the urinalysis gave negative results; the chest microfilm showed a negative picture.

There is a pseudoepitheliomatous hyperplasia of the epidermis which contains a microabscess. In the corium just beneath the epithelium there is a granulomatous infiltrate with epithelioid cells, plasma cells, lymphocytes, and polymorphonuclears, and there is an increase of capillaries. Looking through many sections there are a number of encapsulated yeast-like bodies, which stain strongly with periodic acid-Schiff stain.

Direct microscopic examination and cultures on Sabouraud medium have so far not yielded fungi.

DISCUSSION

Dr. A. W. Stillians: I can report on our case in the Municipal Tuberculosis Sanitarium in which we used stilbamidine. This was the man I presented some months ago with pulmonary tuberculosis and a generalized blastomycosis which caused a large granuloma on the nose and smaller lesions on the cheeks and scalp. The scars still remain. With iodides his condition could be controlled, but as soon as they were stopped his blastomycosis recurred. Then we tried administering stilbamidine (4,4'-stilbenedicarboxyamidine) cautiously and gave him two courses, and today his blastomycosis seems to be healed. The lesions have been absent for over a month, but he has a paresthesia of the face which is due to the use of the drug. That is already clearing. His pulmonary tuberculosis has as yet not yielded to the new nicotinic related drugs.

Dr. M. J. Brunner: On the subject of stilbamidine, I would like to report an experience we had at the University of Illinois Clinics. A patient with blastomycosis who had not been

cured by the administration of large doses of iodine was given one dose of stilbamidine and immediately had a circulatory collapse. It was only with great difficulty that he was revived. On reading up on the subject we found that serious and immediate reactions with stilbamidine are not rare, and the reactions are generally of the type which I mentioned. They may be in the main avoided by slow administraton of the stilbamidine by intravenous drip. A peripheral neuritis such as Dr. Stillians mentioned may develop in the patient.

DR. THEODORE CORNBLEET: Several years ago we presented a patient from our department who had two expansive areas of blastomycosis on the trunk. The surgeon, in discussing the case, said that, in his opinion, the most expeditious manner of resolving the lesions was excision. He went on to say that even a large area for removal is no deterrent if the lesion is a superficial one. Plastic repair would do the rest. Perhaps we should give the surgeons their chance in such a case as this when reasonable medical efforts fail and not let the patient fail because his doctor is a die-hard.

DR. BRUNNER: This same patient was also treated with cautery and an excellent result has been had so far.

DR. JACK RODRIQUEZ (by invitation): Lourie reported on the use of stilbamidine in sleeping sickness. He used this drug in concentrations of 2 mg. per kilogram of body weight. It was used by the syringe technique. He was the first one to report on circulatory collapse. Later, nephrotoxic and hepatotoxic effects of this drug were observed. He also reported anesthesia of the trigeminal nerve.

In August, 1951, Schoenbach reported on the use of this drug in three cases, two of which were systemic blastomycosis. He used it by the slow intravenous drip, 50 mg. for the first two doses, 100 mg. for the next two doses, and 150 mg. subsequently for 10 days, considering the 10-day stretch as one course. He repeated this three times and reported good results in all three cases. He did not mention any toxic effects of this drug. In several instances in which this drug has been used by the slow intravenous drip technique, it seems to be less toxic. However, since fairly good results may be obtained either by surgery or by electrocoagulation, I think it might be best to try these first.

Incontinentia Pigmenti. Presented by DR. ALFRED B. FALK and (by invitation) DR. FRANCIS HETREED.

B. J., aged 6 years, has various-sized areas of macular pigmentation of varying shades of brown on her body extending from head to foot. Her scalp hair is thin. The configuration is not consistent, and the distribution is asymmetric.

At birth the child had no lesions. At the age of 2 weeks she had pneumonia and received therapy with sulfonamides and penicillin. It was at this time that the skin became inflamed, and on subsiding the present findings appeared.

The teeth are affected in the following manner: five deciduous teeth congenitally missing, seven permanent teeth congenitally missing, six deciduous teeth malformed, seven permanent teeth with a malformed appearance.

Mental development is consistent with her age. The Stanford-Binet test revealed an I. Q. of 100.

Eye findings are essentially normal.

The Kahn test was negative. The urinalysis gave normal results. The complete blood cell count gave normal results. The biopsy of the skin lesion revealed an epidermis with a mild degree of hyperkeratosis. High in the dermis are scattered elongated oval cells richly filled with coarse granular pigment.

DISCUSSION

DR. S. W. BECKER: This is a classic case of so-called incontinentia pigmenti. This disorder was discussed in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY by Dr. Epstein and Dr. Pinkus and some others. The name incontinentia pigmenti is really a misnomer because the pigmentary phase of this disorder merely represents a postinflammatory melanosis. I have been reviewing the literature on melanosis of various types for the past few years, and unfortunately it is seldom that the patient's complexion is given. This patient has dark brown eyes, hence she pigments more readily.

This disease is unique because it is sex-limited. There have been about 50 cases reported in the literature and only one or two occurred in boys. In one or two it was stated that the father had the same type of disorder. Most of the patients present other abnormalities. This child presents dental abnormalities. Persons with this disease have congenital cataracts and other retrolental fibroplasia.

The disorder is a nevoid inflammatory disturbance which usually appears very shortly after birth. Sometimes the inflammation is so intense that bullae are present, as in Dr. Epstein's patient. The disorder subsides after a few years, ordinarily when the child is 4 or 5 years of age, and then the inflammatory melanosis fades out. It takes about eight months for the pigment deposit in the chromatophores, as in this case, to be absorbed after the inflammatory phase has subsided. There were, however, two patients reported in whom it persisted, in one into the teens and in the other into the twenties. I do not feel that this child's having had pneumonia with sulfonamide and penicillin therapy had anything to do with the disorder.

Urticaria Pigmentosa. Presented by Dr. Michael Ebert, Dr. Vera Leaf, and (by invitation) Dr. J. F. Sickley.

The patient is a 4-year-old Negro girl. The mother states that the child has had a skin eruption since she was 3 days of age. The eruption began as small papular lesions that disappeared, leaving hyperpigmented spots. As older lesions disappeared, new lesions continued to appear.

The child often complains of itching, and the mother has noted that when the skin of the child was scratched or traumatized, red urticarial lesions would develop at the sites involved.

At present the patient has a generalized spotty hyperpigmentation of the skin. About the arms, shoulders, and chest there are multiple papular lesions. At times small papular urticarial lesions have been observed, but urticarial lesions could not be produced by stroking the lesions.

A biopsy showed urticaria pigmentosa.

DISCUSSION

Dr. Julius E. Ginsberg: There are several things that should be mentioned about such cases. First, they are primarily connective tissue tumors rather than pigment cell anomalies. The pigmentation is only secondary. The tumors disappear as the children approach adulthood. Microscopically, very little infiltrate is seen. Mast cells are difficult to find. This child had vesiculation and bulla formation up to the age of 6 months. That is extremely rare. Dr. Louise Tavs reported on this in the Archives of Dermatology and Syphilology in about 1947. Itching is still present in these extensive lesions. It is well controlled by antihistamines. Sometimes it is difficult microscopically to differentiate mast cells with polychrome methylene blue stain. In these cases the May-Grünwald-Giemsa stain demonstrates the mast granules well. The McManus stain shows that the mast cells contain polysaccharide granules, which are probably the result of the use of heparin. The use of heparin would account for the urtication of the lesions when rubbed.

Dr. Allan L. Lorincz (by invitation): For over six months now the man I presented with urticaria pigmentosa has been taking daily 100 mg. of toluidine blue orally in capsule form without toxic manifestations of any sort. His itching remains subjectively well controlled, even though the lesions persist and urticate slightly on rubbing. I plan to try placebo substitutes for toluidine blue to decide whether the marked subjective relief from itching merely reflects the patient's enthusiasm for a new treatment.

Dr. M. R. Caro: I wish that someone with a large experience in these cases and with a good social service connection would follow up these patients in later life. I have seen a number of cases of urticaria pigmentosa in adult life, and all of them began in adult years. I should like to know whether any of these cases of juvenile urticaria pigmentosa persist into adult life.

Dr. A. H. Slepyan: I agree with the diagnosis of urticaria pigmentosa. The diagnosis is relatively simple when seen in an established case, but coming on suddenly in an adult the picture can be quite unusual. Recently, I had the opportunity of observing a 16-year-old boy who came in with the picture of telangiectasia macularis eruptiva perstans. He showed

dermatographism with marked urtication of the macular lesions. Within two weeks of the onset of his eruption the telangiectatic lesions became purpuric, and the eruption then suggested the angiomatous disorder described by Oppenheim and Yacculo following the use of tripelennamine (Pyribenzamine). Here again, the purpuric lesions showed urticarial lesions on rubbing. Two months after the onset of the eruption, the purpuric lesions began to fade into telangiectatic macules once again. The macular areas urticate profusely, and clinically the picture strongly suggests urticaria pigmentosa. A careful probing history revealed that an antihistamine bought over the counter was taken for a cold two days prior to the onset of the eruption. Histologically mast cells were seen, but they were not as numerous as seen in urticaria pigmentosa. This case suggests strong linkage between telangiectasis macularis eruptiva perstans and urticaria pigmentosa, as well as the drug eruption as described by Oppenheim.

Lichen Planopilaris (for Therapeutic Suggestions). Presented by Dr. Michael H. Ebert and (by invitation) Dr. Harold M. Spinka.

Pityriasis Lichenoides et Varioliformis Acuta (Mucha-Haberman). Presented by Dr. Edward A. Oliver.

Gluttate Parapsoriasis. Presented by Dr. David Omens (by invitation), Dr. Harold Omens, and Dr. J. F. Sickley.

Bullous Syphilide or Haberman's Disease? Presented by Dr. David Omens (by invitation), Dr. Harold Omens, and Dr. J. F. Sickley.

Penicillin-Resistant Syphilis(?) Presented by Dr. F. E. Senear.

Hydroa Vacciniform? Presented by Dr. Milton Robin.

Case for Diagnosis (Hydroa Estival?). Presented by Dr. Michael H. Ebert and (by invitation) Dr. Harold M. Spinka.

Toxic Dermatitis Resembling Acute Disseminated Lupus Erythematosus. Presented by Dr. F. E. Senear and Dr. J. B. Haeberlin Jr.

Scleredema of Buschke? Presented by Dr. P. K. Weichselbaum and (by invitation) Dr. Leonard Becker.

Darier's Disease. Presented (by invitation) by Dr. Allan L. Lorincz.

Lupus Erythematosus (Disseminate?). Presented by Dr. James Webster, Dr. Samuel Bluefarb, and (by invitation) Dr. Stefan Bielinski.

Syringoma. Presented by Dr. Herbert Ratiner, Dr. Harold Rodin, and (by invitation) Dr. Stefan Bielinski.

Localized Myxedema. Presented by Dr. James Webster, Dr. Samuel Bluefarb, and (by invitation) Dr. Stefan Bielinski.

Ocular Pemphigus. Presented by Dr. David Omens (by invitation), Dr. Harold Omens, and Dr. J. F. Sickley.

NEW ENGLAND DERMATOLOGICAL SOCIETY

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Joseph Goodman, M.D., *Secretary*

April 16, 1952.

Verrucous Nevus? Verruca Plana Juvenilis? Presented by Dr. Leo Koretsky, Boston.

H. A. S., a 24-year-old man student, has had an eruption on the right side of the chin for three years. On the right side of the chin extending halfway along the mandible and to the undersurface of the chin there are numerous red tiny (1 to 2 mm.) papules, closely grouped in the central area, more thinly spaced in the periphery.

DISCUSSION

Dr. Joseph Goodman, Boston: The question of treating warts with mercury interests me. Some years ago, I had occasion to look up the original reference to the use of yellow oxide of mercury in treating warts, as well as the original use of neoarsphenamine and other arsenicals. A curious situation was revealed, namely, that all these remedies came from old-time dermatologists who were engaged in treating syphilis. They made an observation that while the patient was receiving mercury for syphilis, the warts disappeared. Thereupon the remedy was given to a number of patients, and in a number of instances the warts disappeared.

The question then arises, "Are any of these remedies efficacious?" In an attempt to answer that question, Dr. Arthur Greenwood and I some years back gave patients injections of saline

and compared the efficacy of that remedy with intramuscular bismuth, which was then reported to be helpful in curing warts. We discovered, in a very small but controlled series, that the two were about equally effective.

It is my opinion that none of these local treatments, other than destructive measures, are effective in treating warts. I should like to go on record as being opposed to the use of mercury, arsenicals or other such remedies in treating warts.

I am of the opinion from the appearance of the lesion that this may be a verrucous nevus. It is limited to one side. The history indicates that it came out in the area in which it is now present and has not shown new areas of involvement.

Multiple Gummata (Healed), Asymptomatic Neurosyphilis, Prozone Phenomenon. Presented by DR. BERNARD APPEL, Lynn, Mass.

In a 42-year-old American Indian woman, M. S., ulcers developed three months ago on the left side of the forehead, on the back of the neck, and on the dorsum of the right foot. The lesion on the forehead was 7 by 5 cm. in diameter and presented a serpiginous border. The two other lesions were 2 by 3 cm. in diameter. The findings of the neurological examination were negative.

Cerebrospinal fluid examination showed no cells; total proteins were 28 mg. per 100 cc.; the colloidal gold curve was 2223322000, and the Davies-Hinton test gave a positive reaction. Reactions to serological tests of blood varied from negative to positive in a dilution of 1:256, with a definite prozone phenomenon.

The patient received 13,000,000 units of penicillin over a three-week period. The skin lesions healed completely in two weeks.

DISCUSSION

DR. CHESTER N. FRAZIER, Boston: It seems to me it is a case of healing syphilitic gummata of the skin. There is one question which might be raised concerning the diagnosis of asymptomatic neurosyphilis, based entirely upon positive reactions to serologic tests. In this part of America, it would seem that precipitation tests are used at present almost entirely on spinal fluid. I think, in general, it has been held that this is not the ideal test to apply when spinal fluid is being examined, as it is not entirely reliable. One might wonder whether this positive reaction which the patient has in the spinal fluid is valid. Of course, the diagnosis of neurosyphilis must rest on that, but it is true that patients with gummatous disease of the skin or skeleton system do have asymptomatic involvement, although rarely is there symptomatic neurosyphilis.

DR BERNARD APPEL, Lynn, Mass.: There is here the question of interpretation in spinal fluid examination. We must not forget that patients with gummata certainly can have evidence of cerebral spinal involvement if a positive cerebrospinal fluid indicates cerebrospinal pathology.

I cannot let this opportunity go by without saying something about the tests on the blood serum. In Massachusetts for the past few years many of us have encountered the very difficult and confusing situation of continually conflicting reports of serological tests. We have here still another phenomenon which is very interesting, the so-called prozone phenomenon, in which the qualitative reaction gives a negative report and the quantitative test gives varying reports. The reactions to the first and second and third dilutions may be negative, but reactions to succeeding dilutions are positive. This finding must make us cautious in discarding a diagnosis of syphilis which we make clinically, but which may not be supported by serologic tests.

Poikiloderma of Civatte. Presented by DR. F. RONCHESE, Providence, R. I.

M. McG., a 61-year-old press operator, has had a reticulated gray discoloration of the forearms for eight months and of the face and neck for three months. Associated with this change is atrophy and telangiectasis. Biopsy shows a picture of changes consistent with the above diagnosis.

DISCUSSION

DR. BERNARD APPEL, Lynn, Mass.: I think that the general clinical picture is so characteristic that the diagnosis cannot be very seriously questioned. I should like, however, to point out several minor elements in this case that are of some interest to me. One is that there definitely seemed to be much more pathology, particularly from the standpoint of pigmentation, on the left side than on the right. The patient reported that during the course of her work she was exposed to more sunlight on the left side of her body than on the right. Also, it may be important to note that she is exposed to small amounts of oil in her work. Even though her contact may be relatively minor, there may be photosensitization of areas exposed to petroleum products.

Lupus Erythematosus? Presented by DR. HARVEY B. ANSELL, Portland, Maine.
Basal Cell Epithelioma, Mucous Cyst. Presented by DR. FRANCIS M. THURMON, Boston.
Epithelioma Adenoides Cysticum. Presented by DR. WILLIAM J. MACDONALD, Boston.
Intraepidermal Carcinoma. Presented by DR. MILDRED L. RYAN, Brockton, Mass.
Lupus Erythematosus Discoides et Disseminatus Chronicus. Presented by DR. JULIUS PICARD, Fall River, Mass.
Nonspecific Granulomata. Presented by DR. WILLIAM J. MACDONALD, Boston.
Dermatomyositis. Presented by DR. EDMUND F. FINNERTY, Boston.
Xanthoma Eruptivum. Presented by DR. BERNARD APPEL, Lynn, Mass.
Dermatitis of Breasts. Presented by DR. MILDRED L. RYAN, Brockton, Mass.
Impetigo of Bockhart. Presented by DR. F. RONCHESE, Providence, R. I.
Keloids. Presented by DR. MARGARET HUSSEY, Quincy, Mass.
Gumma of Skin? Pyogenic Ulcer? Presented by DR. EDMUND F. FINNERTY, Boston.
Pemphigus Vulgaris Acutus. Presented by DR. PAUL J. CATINELLA, Boston.
Lymphatic Leukemia. Presented by DR. FRANCIS M. THURMON, Boston.
Lymphoma, Mycosis Fungoides? Presented by DR. FRANCIS M. THURMON, Boston.
Chronic Lymphedema, Milroy's Disease? Presented by DR. WILLIAM J. MACDONALD, Boston.
Histiocytic Leukemia. Presented by DR. PAUL J. CATINELLA, Boston.
Mongolian Spot, Nevus? Presented by DR. WILLIAM WOLF, Lowell, Mass.

Obituaries

SIMPSON M. MARKSON, M.D.
1883-1952

Dr. S. M. Markson, Clinical Professor and Director of the Department of Dermatology at Marquette University School of Medicine from 1920 to 1951, died at his home on Nov. 17, 1952. His death was attributed to heart disease.

Dr. Markson was born in Glen Robertson, County of Glen Garry, Ontario, Canada, on Jan. 14, 1883. His primary education was obtained in the parochial schools of his native County. In his youth he was very active in sports, playing halfback on the championship Ontario soccer team and being chosen for the "All Star" team. He graduated from McGill University Faculty of Medicine School in Montreal in 1904, following which he worked for a railroad in Chicago to enhance his finances. As a result of his railroad connections he set up practice for a short period at Kenyon in Indian territory in what is now the State of Oklahoma.

In 1906 he was married to Rose Primakow and moved to Milwaukee, where he established himself in general practice. During this period Dr. Markson became interested in dermatology and despite the manifold duties of general practice spent considerable time serving the free clinical dispensaries in Milwaukee as well as making frequent visits to the clinics available in Chicago, especially those under the direction of Dr. Hyde and Dr. Montgomery. Shortly after World War I Dr. Markson gave up his general practice and spent some time in Europe studying chiefly at the University of Vienna under Dr. Finger and at the Herxheimer Clinic.

On his return in 1920 he was made Professor of Dermatology at Marquette University School of Medicine, a position he held until 1951, at which time he became Professor Emeritus. He was associated in the practice of his specialty with his son, Dr. Leonard S. Markson.

Dr. Markson was a member of his local County, State, and National general Medical Organizations, as well as a charter member of the Milwaukee Dermatological Society, the Milwaukee Academy of Medicine, and the American Academy of Dermatology and Syphilology.

"Sim," as he was affectionately known by his colleagues, was a gentleman of the old school, gracious and friendly. Patients loved him for his kind, gentle, tactful speech and manner. His years of general medical practice fitted him well as a teacher, especially in his ability to correlate the dermatological manifestations of systemic disease. His students were enthusiastic about his lectures, which he spiced with quotations from classical English, French, and German literature. He directly stimulated interest in dermatology of several present-day dermatologists,

including the author. His humility undoubtedly accounted for his few contributions to the literature, as he deemed his efforts unworthy because of inferior quality.

Dr. Markson was a slender, rather frail-appearing man, impeccable in his dress. He was a brilliant conversationalist and particularly delighted in relating episodes in his early life, especially those pertaining to the partnership of his father with a canny Scot in a general merchandise store and of his parochial school experiences in rural Canada. Dinners out or at home would be highlighted by the serving of a *Pousse Café*, always accompanied by French Provincial stories in dialect as only he could tell them.

Dr. Markson lived without ostentation, but he contributed much to the world he lived in and he will be well remembered.

MAURICE J. REUTER, M.D., Milwaukee.

Obituaries

MAX SCHEER, M.D.
1883-1953

American dermatology lost an outstanding representative when Dr. Max Scheer died on March 1, 1953, at the age of 69, of coronary disease. He is survived by three brothers, Moe, Joseph, and Samuel, and a sister, Mrs. Rose Saffir.

Dr. Scheer was born in Zaranow, Austria, on Nov. 1, 1883. He came as a child to the United States, where he attended a New York City public school. He graduated from the College of the City of New York in 1901 and obtained his medical degree from the College of Physicians and Surgeons in 1905. From 1909 to 1916 he was in general practice and served at the Health Department from 1917 to 1921. At one time he was connected with the Harlem Hospital.

After a three-year internship at Mount Sinai Hospital, from 1905 to 1908, he joined the staff of that hospital and served in the department of Dermatology until 1946. Since 1913 he was a member of the Department of Dermatology at the Vanderbilt Clinic, and in 1926 he went with a group of men under Dr. George M. MacKee to the Post-Graduate Medical School and Hospital, and later, in 1934, to the Skin and Cancer Unit.

Dr. Scheer retired in 1949 and was at that time Clinical Professor of Dermatology and Syphilology and Chief of one of the services. For many years he was Consultant to the Hebrew Orphan Asylum.

Dr. Scheer was a member of the Metropolitan Medical Society, the New York Academy of Medicine, the American Academy of Dermatology, the American Medical Association, the New York County and the New York State Societies, and since 1922 he was a member of the Manhattan Dermatological Society. He became a Diplomate of the American Board of Dermatology and Syphilology in 1933, as one of the Founders Group.

Dr. Scheer was interested in athletics and for many years was a member of the City Athletic Club, which he attended regularly and where he had many friends. An incident that will long be remembered by many members of the Manhattan Dermatological Society is his wrestling match with the late Dr. Parounagian. In spite of his small stature, Dr. Scheer easily matched the much larger Dr. Parounagian because of his knowledge of jiujutsu. During his long illness the City Athletic Club showed great generosity to Dr. Scheer.

In his youth Dr. Scheer was interested in classical languages, studying Latin and Greek. During the last years of his life he studied Hebrew. He was a student of history and had a large library of historical volumes.

His main hobby, however, was deep-sea and fresh-water fishing, and he was known as an expert fisherman. This hobby took him to Mexico and Canada and to most of the waters of eastern United States.

During his illness Dr. Scheer developed a fine philosophy of life, becoming intensely interested in human beings, and he lost regard for many unimportant features of modern life. This attitude of his was shown by his behavior at Roosevelt Hospital where he was taken during the last coronary attack. He was always cheerful and made friends with the other patients whom he constantly encouraged and advised. All who visited him were impressed with his serene attitude.

Although Dr. Scheer was not a prolific writer, he was an excellent teacher and won the admiration of those who heard his lectures. Many of his students became his friends in later life. His discussions at meetings were interesting and enlightening. His loss will be felt by many, and he will long be missed and remembered by most dermatologists.

WILBERT SACHS, M.D., New York City.
DAVID BLOOM, M.D., New York City.

Books

Atlas de dermatologie: En Couleurs. By P. de Graciansky and S. Boulle. First 4 (of 20) fascicles. 8,000 francs. Loose-leaf Fabrikoid binder. Fr. Librairie Maloine S. A., 27 rue de l'École-de-Medicine, Paris 6e, 1952.

This is an unusual atlas of dermatology that is being printed in 20 fascicles which, when completed, will contain 320 colored plates in five volumes.

The plates, in the form of colored photographs, are by far the best examples of colored dermatologic photographs that the reviewer has seen. They should be excellent for teaching purposes. These are all clinical photographs; opposite each colored plate is a brief clinical description and also, at times, a comment regarding the individual case. Each plate has the diagnosis in French and also in either Latin or English; in addition, a reasonable number of photomicrographs in black and white is included, especially when histopathologic pictures are of diagnostic value.

A concise text presents clinical information and various diagnostic factors, together with prognosis and treatment. The authors have recognized that interpretation, classification, and treatment of various dermatoses and neoplasms differ in various countries. They have referred to these differences and in many places have mentioned by name workers with whom they would agree or those who have different points of view or who use different types of treatment. However, no bibliography is included.

The quality of the paper and type is excellent; the loose-leaf form permits additions to, or changes in, the arrangement of the dermatoses, if desired. Each dermatosis has its own page numbers; the atlas does not have an accumulative, consecutive system of numbering. The Fabrikoid loose-leaf binder for the first volume already shows signs of warping, which is true of copies received by two of my colleagues. It is hoped that this can be corrected in the other four volumes.

The reviewer is of the opinion that the atlas will be worth while for all dermatologists and for those interested in dermatology, if because of no other factor than the excellence of the 320 plates in color, assuming that subsequent illustrations will be as good as those printed thus far. The concise text also can be recommended to the student of dermatology. The authors plan to publish a new fascicle every three months.

Essentials of Dermatology. By Norman Tobias. Fourth edition. Price, $6. Pp. 596, with 186 illustrations, three plates in color. J. B. Lippincott Company, 227-231 S. 6th St., Philadelphia 5, 1952.

The author presents this as a book intended primarily for the medical student and the general practitioner. The book covers the usual spectrum of dermatologic entities. The author gives a clinical description of the disease, as well as a pathologic summary, and includes sections on recent treatment and nursing problems.

The text completely lacks a bibliography. Without such reference to the medical literature, a reader is led to believe that this text represents original observations and work. In addition, this lack of bibliography gives the medical student no ready recourse to further reading on any particular subject. Because of the brevity of the text, no discussion of controversial facts is included. Thus, on occasion, a misinterpretation of the material presented could occur. Although the book contains a rather generous number of pictures, the detail of a large proportion of these is such that the student being introduced to the subject would gain very little appreciation of the dermatologic condition thereby illustrated.

This book is not recommended for the graduate student in dermatology. It may, however, fill a need as an introduction to dermatology for the medical student.

Dermatology: A Textbook for Nurses. By H. Rattner, M.D. Price, $4.25. Pp. 270, with 100 illustrations, seven plates in color. W. B. Saunders Company, Philadelphia, 1953.

Dr. Rattner has written an excellent textbook on dermatology for nurses. The field of dermatology and syphilology is well covered in this book; that is to say, all the major groups of diseases receive attention. Not all the individual diseases in each group are mentioned, of course, but the boundaries are there. The notes on treatment are in the best of taste and are singularly free of overoptimism. There is a great deal of practical information in the various discussions of such common problems as baldness, large pores, hirsutism, cosmetic sensitivity. Any nurse who reads these sections carefully will be able to answer most of the questions about dermatology which her patients might ask. The chapter on eczema is particularly good. The author carefully separates the theoretical problems involved in eczema from the practical ones. It shows the beginner that the subject is a deep and complicated one, but that in most cases the practical aspects are not so complicated.

From the literary aspect, the book is well written. The author's dedication illustrates so well this aspect of his work, "To My Family who have long since learned that there is more to Dermatology than meets the eye." There are passages of humor here and there which a professional author would be proud to have written.

The photographs are generally of high quality, considering that they are black and white (except for a single page in color). As usual, one wishes that there were more illustrations, but Dr. Rattner suggests at the beginning that the book be supplemented with lectures and lantern slides. The book is highly recommended as a textbook for nurses.

CORRECTION

In the Directory of Dermatologic Societies published in the February issue, the Cincinnati Dermatological Society was incorrectly listed as the Cincinnati Society of Dermatology and Syphilology. Dr. Alfred L. Weinger, Union Central Building, Cincinnati, is President, and Dr. Raymond R. Suskind, Kettering Laboratory, University of Cincinnati, is Secretary.

In the article by Dr. Aquilina and his colleagues published in the February issue of the A. M. A. Archives of Dermatology and Syphilology, the first sentence of the fourth paragraph on page 171 should read, "On the maintenance dose of 100 mg. of cortisone by mouth daily, the condition is still in remission and no new lesions have developed."

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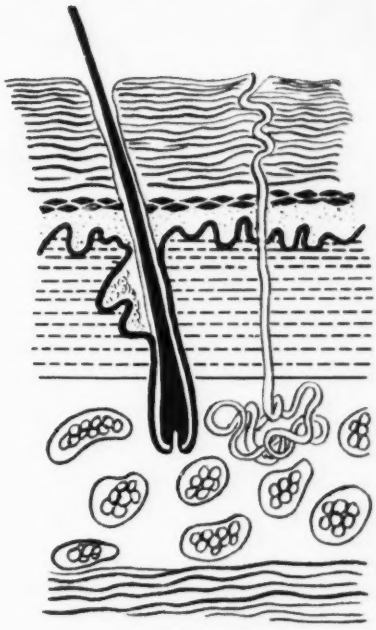

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FACTS ABOUT *Synthetic*

In the short space of five years synthetic detergents have made a tremendous change in the household washing habits of American housewives. At the start of 1948 they accounted for less than 10% of the "laundry soap" business; by the end of 1952 they accounted for over 70%. The product enjoying the greatest popularity in this classification (Tide) is currently being used by one woman out of every four who do their own dishes, and one out of every three who do their own laundry.

For your information the Chemical Division of The Procter & Gamble Company has prepared this article, discussing some of the differences between synthetics and soaps which formerly were widely used for household washing.

How synthetic detergents differ from soaps

Synthetic detergents are organic compounds with molecules whose opposite ends are highly polarized like those of soap; one end consists of the type of structure which is oil soluble, the other consists of the type which is water soluble.

Magnesium and calcium soaps formed by interaction of sodium soaps with water hardness are among the most insoluble of compounds. The precipitation which occurs with soap in hard water wastes soap and causes cloudy glassware and unsightly deposits. The "tailor-made" molecules of synthetics do not form these insoluble compounds in hard water. They, therefore, leave surfaces cleaner because they are free of any precipitated "soap film" formed during rinsing. Also, unlike soaps, in solution, synthetics can be used at almost any pH. Soaps, of course, must be kept at pH 10 or above, or they will split into fatty acids. Most synthetic products in general use have solution pHs from 6.0—10.0. Few are above the pH of soap.

The special washing abilities of synthetic detergents

As a consequence of the characteristics discussed above, synthetics are particularly well-suited for washing off acidic soils which would destroy soap. Since they aren't destroyed by hardness or by salts of other metals as soaps are, they are well-suited to washing a great variety of things which could be washed only with alkalis before—for instance, glass laboratory utensils.

The effect of synthetic detergents on bacteria

The synthetics in general and widespread use have about the same general effect on bacteria as soaps —that is, they have some germicidal effect on some strains, but for creating relatively sterile conditions, synthetic detergents rely more on removing bacteria than on killing them.

Detergents

The effect of synthetic detergents on skin

Over the past seven years Procter & Gamble has included these synthetic detergents in the continuing series of tests, designed to measure the effect of washing products on skin. In addition to the routine patch and arm-immersion tests, Procter & Gamble has conducted, under careful medical supervision, extensive clinical and home-usage tests of all its products, including the new synthetic detergents. These tests indicate that household detergents in use today, as a class, do not differ greatly in their effect on the skin from the general-purpose package soaps which have been used for years. Some have a lower pH than soaps and, hence, less effect on persons sensitive to alkali.

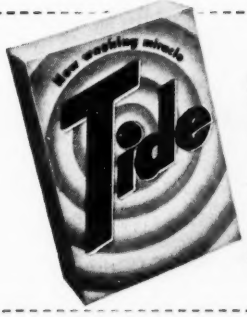
Like soaps, the detergents generally are mild primary irritants, but a fact not generally realized is that on the average person subjected to patch tests or immersion tests, most detergent solutions cause less skin reaction than do soap solutions.

Women have had many years in which to learn whether or not all soaps or certain soaps prove irritating in each particular case. Any problems arising from the effect of soap on skin have, therefore, been spread over decades. In the case of washday detergents, practically every woman in America was exposed to these products in a concentrated period of two or three years.

This great popularity and widespread use of synthetic detergents, together with their relative newness on the market, have resulted in a situation where synthetic detergents are likely to be suspected as the cause of many cases of dermatitis where they probably are not involved at all. With almost all housewives now using synthetic detergents for one or more purposes in their homes, it is inevitable that when a physician sees a case of hand dermatitis, a history of exposure to detergents will be obtainable. The significance of the dermatitis must be appraised against the background of the wide use of the detergent products.

For further information . . .

send for free booklet, "About Synthetic Detergents—Facts for Physicians." Write: The Procter & Gamble Co., Box 687B, Cincinnati 2, Ohio.



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New and Nonoffcial Remedies, 1952: 44

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Archives of Dermatology and Syphilology, Feb., 1949: 243-245
Abdominal Surgery, Bancroft and Wade, 1947: 804

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References:

1. Rothman, J. and Shapiro, A. L.: Med. Clin. N. Amer. 33:274-5, Jan., 1949.
2. Stieglitz, E. J.: Geriatric Medicine, p. 848, 1943.

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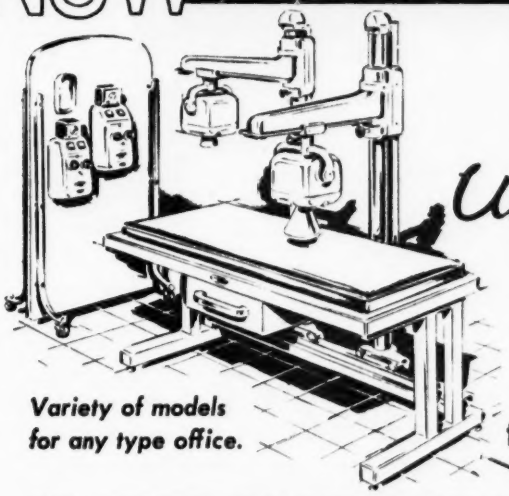

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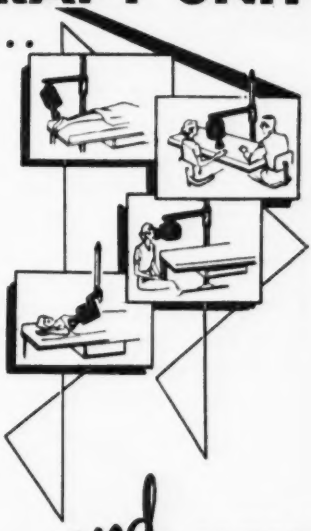

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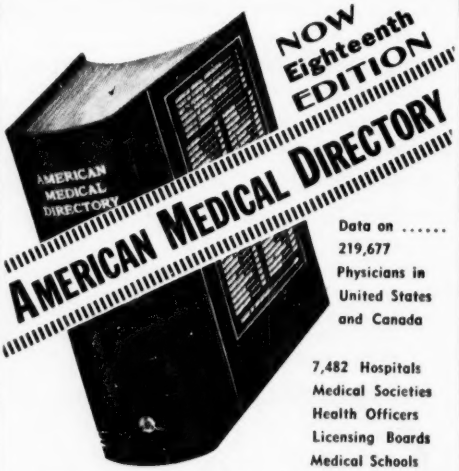

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REFERENCES:

1. Slinger, W. N., and Hubbard, D. M. (1951), Arch Dermat. & Syph., 64:41, July.
2. Slepyan, A. H. (1952), *Ibid.*, 65:228, February.
3. Ruch, D. M. (1951), Communication to Abbott Laboratories.

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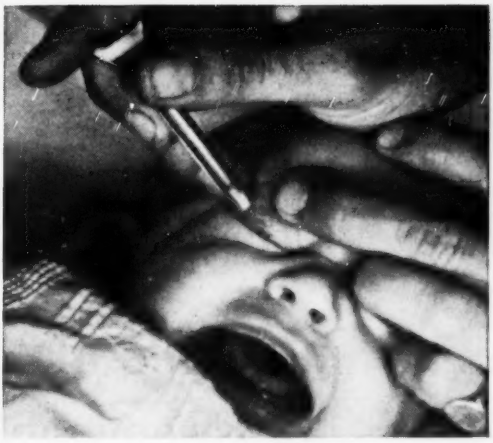

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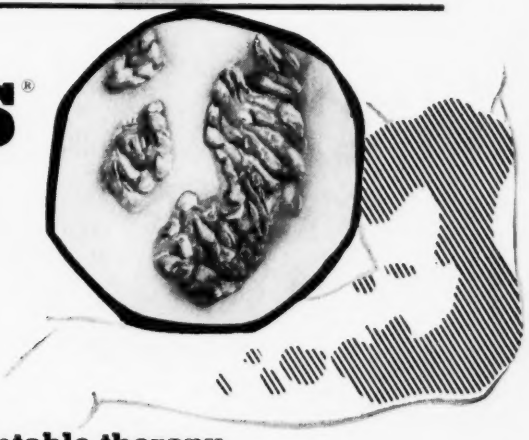

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*Sulzberger, M. B., and Wolf, J.: Dermatology, Essentials of Diagnosis and Treatment, Chicago, Year Book Publishers, Inc., 1952, p. 323.

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